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Health Effects Research Program Fiscal Year 1975-1977 Summary

Interagency Energy-Environment Research and Development Program Report

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To insure that the major health and environmental problems related to energy resource development were anticipated and evaluated on a schedule consistent with technological progress, the EPA-planned and coordinated Federal Interagency Energy/Environment R&D Program was initiated in the latter half of FY74. This document provides an overview of the health effects related component of the Interagency Program. The discussion focuses on the overall principles and objectives of the research effort rather than a detailed discussion of the individual projects.

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ABSTRACT

To insure that the major health and environmental problems related to energy resource development were anticipated and evaluated on a schedule consistent with technological progress, the EPA-planned and coordinated Federal Interagency Energy/Environment R&D Program was initiated in the latter half of FY74. This document provides an overview of the health effects related component of the Interagency Program from an administrative as well as technical perspective. The discussion focuses on the overall principles and objectives of the research effort rather than a detailed discussion of the individual projects.

FOREWORD

This document provides an overview of the health effects research component of the Federal Interagency Energy/Environment Research and Development Program that is being coordinated by the Office of Energy, Minerals and Industry (OEMI) within the Office of Research and Development (ORD) of the United States Environmental Protection Agency (EPA). The information used to generate this document was provided by the project officer, Mr. Gerald Rausa, and consisted of project progress reports (prepared by the principal investigator), applicable Smithsonian Scientific Information Exchange (SSIE) documents, and quarterly, semiannual, or annual project or program status reports (prepared by the appropriate project officer, program coordinator, or principal investigator).

All projects mentioned in this report were described in at least one of the above information sources, but few were described in all three. Since the available information sources were prepared by a large number of individuals, each with a slightly different perspective, the level of detail for any particular project was often not consistent with that describing another project. Within those constraints, the Interagency Energy/Environment health effects related R & D program is presented from several discipline and administrative perspectives.

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1.0 SUMMARY

Under the auspices of the Federal Interagency Energy/Environment Research and Development Program, approximately forty-seven million dollars has been allocated over the past three and a half years in support of research to determine the health impacts associated with this country's accelerated energy resource development and utilization. This document summarizes that continuing energy-related health effects R&D effort.

Pertinent technical and administrative aspects from each of the over one hundred eighty research projects are furnished in the Appendix. Research synopses are provided at the project-aggregate and program level in a manner that conveys the status and direction of the health effects related Interagency R&D Program to date.

1.1 R&D OVERVIEW

As the nation strives to reduce its dependence on foreign sources of energy, increased attention has focused upon the health and environmental problems arising from intensified domestic resource development and utilization. On the Federal level, the recognition of this issue resulted in the formation in 1974 of the Interagency Energy/Environment Research and Development (R&D) Program, whose principal goal was to insure that major health and environmental problems related to resource development were anticipated and evaluated on a schedule compatible with energy technology development and commercialization.

The program is administered and coordinated by the U.S. Environmental Protection Agency's (EPA) Office of Energy Minerals and Industry (OEMI), within the Office of Research and Development (ORD). The program utilizes an extramural implementation approach, with EPA relying heavily on expertise available within other Federal agencies. The overall R&D effort encompasses two main subdivisions:

- R&D to define the effects of energy-related pollutants on man and the environment
- R&D to develop technological measures for controlling the release of these pollutants to the environment.

A substantial portion of the first subdividion is devoted toward determining the human health impacts of energy-related pollutants or activities. Research within this health effects effort is organized according to five categories or objective areas, as defined by the King-Muir Report:*

- Identification of hazardous agents
- Dose and damage indicators
- Metabolism of hazardous agents
- Evaluation of hazards to man
- Damage, repair, and recovery mechanisms

The health effects related research currently emphasizes pollutants associated with fossil fuel combustion (both conventional and advanced), coal conversion, and energy conservation efforts. In relation to human health, the program focuses on those agents whose effects

*Final Report of the Interagency Working Group on Health and Environmental Effects of Energy Use (King-Muir Report) prepared for OMB and CEQ, November 1974.

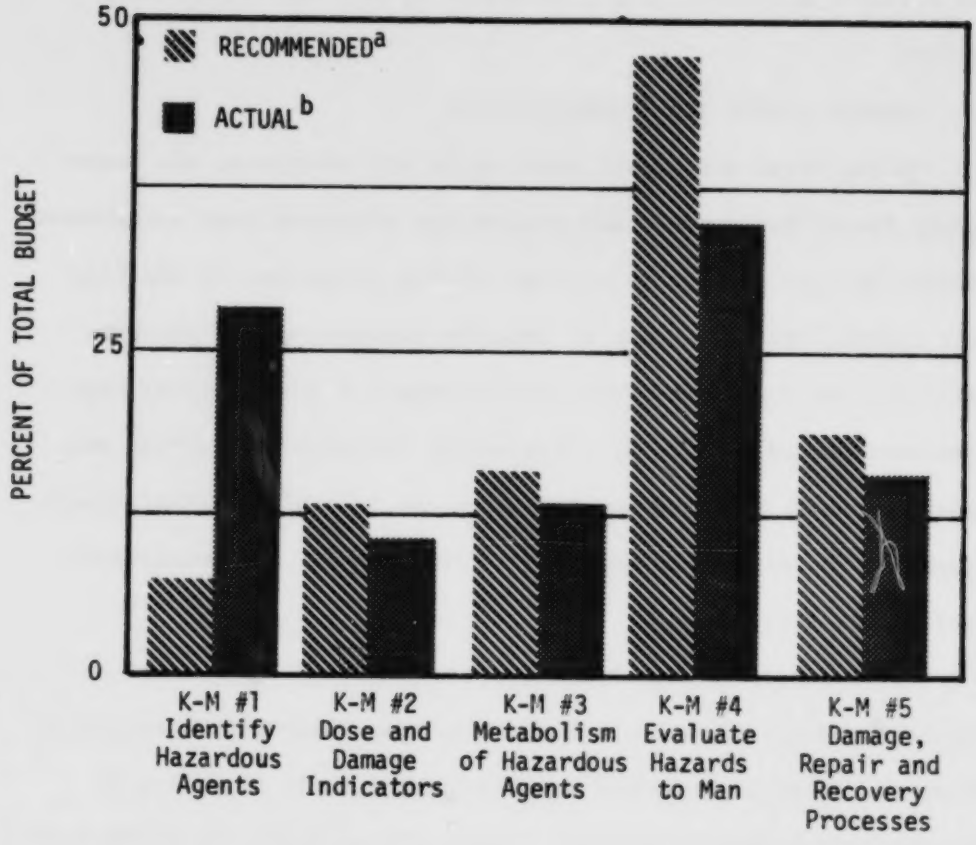
gives rise to carcinogenesis, mutagenesis, teratogenesis, toxicity, and system dysfunction (e.g., disorders of the cardio-pulmonary system).

1.2 PROGRAM STATUS AND ACCOMPLISHMENTS

In the three and a half years since its inception, the Inter-agency Energy/Environment R&D program has allocated over forty-seven million dollars for health effects related research. In the King-Muir report, the allocation of research emphasis within the five objective areas was implied in the recommended funding level over a five-year period (FY 75-79). The actual research efforts* to date appear to have diverged somewhat from the initial King-Muir Report blueprint if temporal aspects of the research are not considered (see Figure 1-1).

The apparent discrepancies between suggested and current research emphasis appear to be associated with King-Muir Objective #1 (identification of hazardous agents) and King-Muir Objective #4 (evaluation of hazards to man). These discrepancies are perhaps to be expected, since the research program incorporates a hierarchial approach in the identification and assessment of hazardous pollutants. In the early stages, research is directed toward screening the large number of energy-related pollutants for hazardous species; once identified, those high priority pollutants are then subjected to more intensive investigation to define the actual hazards to man.

*Based on actual FY 75-77 project funding, as allocated; funds of projects spanning several objective areas are allocated equally.



a based on recommended FY 75-79 K-M objective area funding, as specified in the King-Muir Report

b based on actual FY 75-77 project funding, as allocated; funds of projects spanning several K-M objective areas were allocated accordingly (see Table A-1)

Note: Apparent discrepancies reflect temporal aspects of the research program (see text for explanation)

FIGURE 1-1
COMPARISON OF RECOMMENDED AND ACTUAL RESEARCH EMPHASIS ACROSS KING-MUIR OBJECTIVES

Since the Interagency Energy/Environment R&D Program was originally designed to complement the existing R&D program within each of the participating agencies, it is often difficult to assign specific accomplishments to either sector. However, there are a number of achievements that can be either partially or wholly attributed to the health effects related Interagency effort. Rather than citing specific research results, the Interagency Program should be viewed from a larger perspective. Taken in aggregate, these research efforts to date have produced a number of significant accomplishments.

A variety of pollutant species are being examined for their adverse impacts on human health; and in particular, those pollutant species normally associated with fossil fuel combustion (e.g., SO_x, NO_x, O_3, particulate material). Recent research efforts have confirmed that these pollutants and some of their atmospheric reaction products are detrimental to human health. Sufficient evidence has been accumulated to require a reassessment of current air quality standards for a number of the criteria and non-criteria air pollutants. The Interagency Program has contributed significantly to this research effort.

A major focus of the Interagency R&D effort has been to assess the potential health impacts of developing energy technologies. Although a number of preliminary assessments have been made, most of the data are derived from processes in the early stages of development. The Interagency Program recognizes that any standard setting

- Pharmacokinetic and toxication-intoxication studies - increased emphasis upon understanding these mechanisms is crucial for prediction of the potential hazards of energy-related compounds.

- Organ toxicity studies - current laboratory and clinical studies are unable to reliably determine developing organ damage at a point where that damage is reversible. The major need in this area is for tests able to detect very early organ damage and to determine the implication of such changes with respect to health effects.

- Mutagenic and carcinogenic effects studies - additional effort must be directed to the actual screening of potentially hazardous materials as well as the development of sophisticated experimental procedures required to test various pollutant classes.

- Teratogenic and reproductive effects studies - new, rapid and reliable tests to define subtle teratogenic and reproductive risks are required.

- Behavioral and neurotoxic effects studies - energy related pollutants or activities need to be evaluated for subtle neurobehavioral changes resulting from low-level chronic exposures to toxicants, especially in the occupational environment.

- Synergistic and other interactive studies - the ability to define and predict biological responses resulting from stresses applied in combination (i.e., antagonistic or synergistic interactions) is needed.

- Inhalation toxicity studies - further studies are required to define the risks associated with inhaled pollutants, and especially methods to define actual integrated absorbed doses (as opposed to "exposure doses").

- Epidemiological, clinical and medical surveillance studies - efforts should be directed toward the medical surveillance and identification of occupational or other high risk groups.

- Extrapolation from animals to man and standards development - the refinement of risk extrapolation from cellular or animal systems to man is obvious, when one considers the amount of materials that require testing in relation to the limited testing resources currently available. Efforts in developing the ability to reliably extrapolate risks to man requires immediate attention.

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2.0 BACKGROUND

As the United States attempts to satisfy its increasing need for energy while reducing its dependence on foreign energy sources, energy-related health and environmental problems arising from domestic energy development and use become increasingly important. To insure that major health and environmental problems related to energy resource development are anticipated and evaluated on a schedule compatible with energy technology development and commercialization, two Federal Interagency Working Groups* representing 23 departments and agencies were convened in 1973-74 during the planning phase of the Federal energy development programs. These Working Groups developed a program structure for a Federal interagency research and development effort that would assess potential health and environmental effects of accelerated energy development and perfect pollution control measures to minimize the associated environmental impacts. In addition to the program structure, the Working Groups also defined specific goals and recommendations for the Interagency Energy/Environmental Research and Development (R&D) program which were stimulated by the December, 1973 report of the Ray Committee

*Interagency Working Group on Health and Environmental Effects of Energy Use; Interagency Working Group on Environmental Control Technology for Energy Systems.

(The Nation's Energy Future) and which served as a basis for a special Congressional appropriation for environmental R&D related to energy development.

The Interagency Energy/Environment R&D Program is administered and coordinated by the U.S. Environmental Protection Agency's (EPA) Office of Energy, Minerals, and Industry (OEMI), within the Office of Research and Development (ORD). In order to maximize its useful output, the program utilizes an extramural implementation approach, with EPA relying heavily on expertise available within other Federal agencies. Research activities are performed by more than a dozen Federal agencies in addition to EPA. The overall effort is subdivided into two major parts:

- R&D on effects of pollutants, including health effects, ecological effects, pollutant characterization and measurement, pollutant transport and fate, and integrated assessment of all types of effects.*
- R&D on technological measures for controlling the release of pollutants to the environment, including changes within an energy extraction, conversion or utilization process as well as end-of-system control measures.**

The R&D program recognizes the need to initiate research now in order to develop the health and ecological effects data base

*Described in the Final Report of the Interagency Working Group on Health and Environmental Effects of Energy Use (King-Muir Report), prepared for the Office of Management and Budget and the Council on Environmental Quality, November 1974.

**Described in the Final Report of the Interagency Working Group on Environmental Control Technology for Energy Systems (Gage Report), prepared for the Office of Management and Budget and the Council on Environmental Quality, November 1974.

necessary to support environmental quality standards and source discharge regulations addressing energy technologies that will not be commercially available before 1985 or 1990. Within the health and environmental effects component, the Interagency Energy/Environment R&D Program incorporates an implementation strategy that addresses short, intermediate, and long-term research needs: the short-term need to support regulatory actions, the intermediate-term need to define the problem areas, and a long-term need to prevent health and environmental damage rather than merely to regulate it. Within that implementation strategy, the criteria for determining research priorities include the following:

- potential magnitude and importance of the health/environmental impacts;
- nature and potential utility of the technology;
- expected rate of development/utilization of the technology.

Within this framework, the R&D program must present the clearest possible statement of the nature and extent of actual and potential changes in the human environment associated with ongoing and proposed energy development. The health effects related portion of the Interagency Energy/Environment R&D Program figures prominently in that effort.

2.1 HEALTH EFFECTS R&D OVERVIEW

The energy-related health effects R&D effort is designed to provide the data base necessary to assess the health impact of

enhanced energy production and use on a schedule that is consistent with energy technology development and commercialization. It is organized according to five categories or objective areas as defined in the King-Muir Report, namely:

Objective #1: Identify hazardous agents - to utilize simple, inexpensive and reliable biological assay systems in detecting the presence of toxic, carcinogenic, mutagenic, and/or teratogenic agents associated with energy-related activities.

Objective #2: Dose and damage indicators - To develop more rapid and sensitive biological methods to detect and quantify early, sublethal, reparable changes to various target organs or systems.

Objective #3: Metabolism of hazardous agents - To define the routes and rates of incorporation, metabolism, deposition and elimination of hazardous agents in order to specify tissues, organs, and functions at risk.

Objective #4: Evaluation of hazards to man - To quantitatively evaluate short- and long-term hazards to man (normal, susceptible and stressed populations) through simultaneous exposures to combinations of stresses associated with energy activities

Objective #5: Damage, repair, and recovery processes - To determine the processes of damage, repair, recovery, protection, and amelioration in biological systems exposed to hazardous agents associated with energy technologies

Four governmental units are participating in the health effects related component of the R&D Program - The Environmental Protection Agency (EPA), The Energy Research and Development Administration (ERDA), The National Institute of Environmental Health Sciences (NIEHS), and the National Institute for Occupational Safety and

Health (NIOSH). Since the Interagency R&D program was designed with each participating agency's base research program in mind, the additional funding from the Interagency program (often referred to as the EPA "pass-thru" program) supports energy-related research that complements the existing research efforts of each participant. Health effects related research areas not only reflect the current priorities assigned to the various energy technologies but also the participating agencies' perspectives as defined by their legislative mandates.

The health effects related research currently emphasizes the health problems associated with fossil fuel combustion (both conventional and advanced), coal conversion, and energy conservation efforts. Problems associated with alternate energy sources are also being considered because portions of research efforts are directed to generally applicable methods development and fundamental research. In relation to human health, the program emphasizes those agents whose effects give rise to carcinogenesis, mutagenesis, teratogenesis, toxicity, and system dysfunction (e.g., disorders of the cardiopulmonary system).

2.2 OBJECTIVES

Under the auspices of the Federal Interagency Energy/Environment Research and Development Program, approximately forty-seven million dollars has been allocated over the past three and a half years in support of research efforts to obtain the data necessary to

reliably estimate the potential health effects associated with this country's accelerated energy resource development. This document summarizes that continuing energy-related health effects R&D effort from an administrative as well as a technical perspective. The specific objectives of this report are:

- to integrate the available information describing all health related projects supported by the Interagency Energy/Environment R&D program (since its inception) into a comprehensive format,
- to summarize that information in a manner that succinctly conveys the status and direction of the health effects related Interagency Program to date.

In this summary of the health effects related program, several constraints must be recognized. The information used to prepare this document was derived from project progress reports (prepared by the principal investigator), applicable Smithsonian Scientific Information Exchange (SSIE) descriptions, and quarterly, semi-annual, or annual project or program status reports (prepared by the appropriate project officer, program coordinator, or principal investigator). All projects mentioned in this report were described in at least one of the above information sources, but few were described by all three. Since the available information sources were prepared by a large number of individuals, each with a slightly different perspective, the level of detail for any particular project was often not consistent with that describing another project. The inconsistencies within each information category (i.e., project reports, SSIEs, or status reports),

coupled with the limited coverage for many projects, made it difficult to assess the overall progress of each individual research effort since its inception. However, the available information does allow the presentation of a general overview of the health effects related research program at the project-aggregate and program level.

2.3 APPROACH

All health effects related research projects that have been supported by the Interagency Energy/Environment R&D Program, since its inception, have been identified in the available information sources, examined, and categorized according to a number of pertinent research factors. These factors, which include administrative details (e.g., project officer, principal investigator, planned period of performance), relevant areas of scientific research (e.g., King-Muir category, health end point), and applicable technological emphasis (e.g., pollutant, media, energy technology), have been provided in the Appendix for all research projects (see Table A-1). All information included in that project listing was obtained from the available project documentation. Under a given research heading (e.g., K-M sub-objective area), a particular project may be classified more than once if it contains aspects pertinent to those multiple classifications.

Since the Interagency R&D program is designed to complement existing research efforts within the participating agencies, it is necessary to examine the health-effects related program from those

perspectives. With that in mind, five research disciplines have evolved that describe the Interagency effort in dimensions more familar to the base programs of each of the four participating agencies. Those research disciplines include the following:

- Bioscreening - the development and utilization of rapid, accurate, and inexpensive biological assay systems (in vitro and in vivo) to examine large numbers of energy-related materials for the presence of hazardous species.

- Cellular Toxicology - the development and utilization of cell or tissue cultures to define the type, mechanism of action, recovery and repair processes, and extent of biological activity associated with test materials.

- Animal Toxicology - the determination of quantitative dose-response information of biologically active materials in whole animal systems.

- Human Health Studies - the identification and quantification of health risks of hazardous materials through the use of toxicological, clinical, and epideminological studies of human subjects.

- Risk Assessment/Data Extrapolation - the development and utilization of statistical methods to estimate health risks associated with individual or population exposure to hazardous materials (e.g., species-to-species comparisons, low-dose extrapolations).

The five research disciplines are not discreet units, but rather contain a certain degree of overlap. Classification of the health effects-related research projects according to the five research disciplines are specified in the Appendix (see Table A-1).

In order to describe the association between applicable King-Muir objective areas and research disciplines, Figure 2-1 has been developed. In that figure, the amounts of overlap between K-M objective areas and each research discipline are provided, along with the proportion of the total research program that each represents. In developing Figure 2-1, individual projects were cross-referenced between K-M objectives and research discipline (according to Table A-1 in the Appendix), while the percent of effort was equated to that particular entry's proportion of the total research funds authorized to date.* When a project pertained to several classifications, funds were distributed equally across the relevant areas. Figure 2-1 permits one to rapidly identify the pertinent K-M objective areas representative of a particular research discipline.

The remainder of this document describes the Interagency health effects-related R&D efforts in terms of the five research disciplines. The ensuing discussions focus on the overall principles and objectives of the research effort rather than a detailed discussion of the individual projects.

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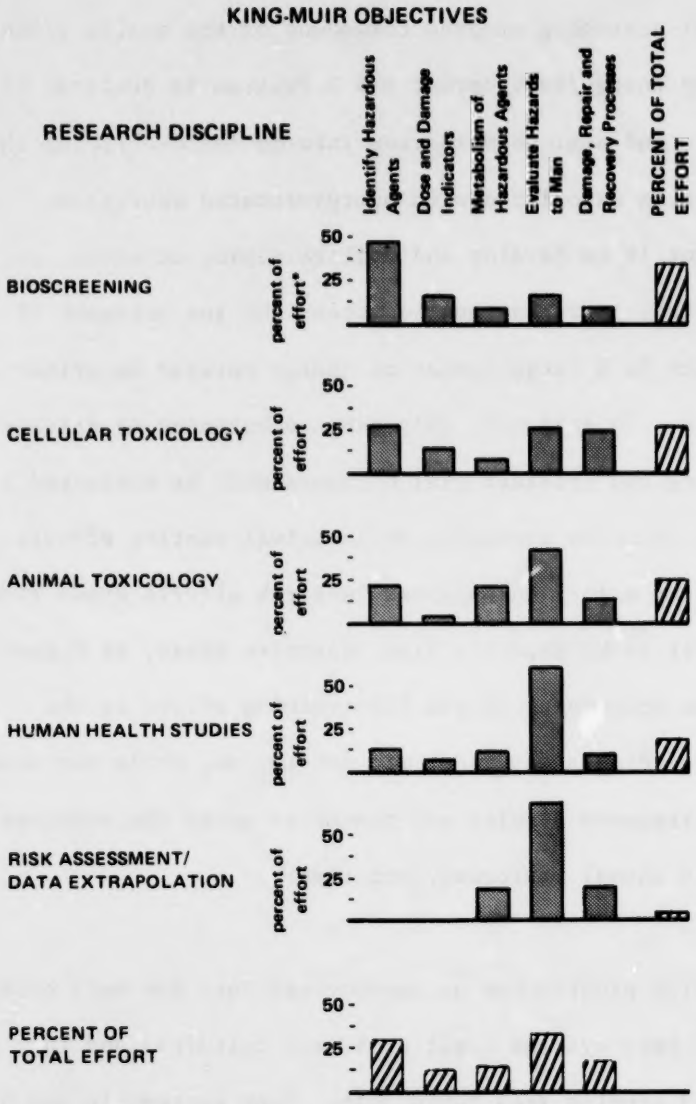
*FY 75 - FY 77



*based on allocated funding; see Table A-1 in Appendix for actual project-by-project coverage

FIGURE 2-1
DISTRIBUTION OF RESEARCH DISCIPLINES ACROSS KING-MUIR OBJECTIVES

3.0 BIOLOGICAL SCREENING PROGRAM

The biological screening program component of the health effects related Interagency Energy/Environment R & D Program is designed to provide qualitative and semi-quantitative information describing the adverse health impacts associated with energy-related activities. The program's intent is to develop and utilize rapid, accurate, and inexpensive biological assay systems to screen for the presence of hazardous components in a large number of energy related materials or effluent streams. In this way, only those substances or streams identified as posing the greatest health hazard will be subjected to the more expensive and time consuming whole animal testing efforts.

The bioscreening effort encompasses research efforts drawn from all of the King-Muir (K-M) Report's five objective areas, as Figure 2-1 indicates. The main focus of the bioscreening effort is the identification of cytotoxic and genotoxic substances, while the more quantitative dose-response studies are conducted under the auspices of the cellular and animal toxicology programs.

3.1 OVERVIEW

The bioscreening program can be categorized into two main areas; *in vitro* (isolated test systems, cell or tissue cultures) and *in vivo* (whole animal) studies (see Table 3-1). Test systems in use or under development examine a variety of targets (e.g., microorganisms,

TABLE 2-1

BIOSCREENING TEST PROGRAM

RESEARCH AREA	TEST SYSTEM	RESPONSE INDICES
MICROBIAL SCREENING	Bacterial (*Salmonella typhimurium*) (*Saccharomyces cerevisiae*)	Mutagenicity (base pair substitution, frameshifts, with/without metabolic activation)
	Bacteriophage (QB, ØX174)	Replication inhibition
IN VITRO SCREENING	Mammalian cell cultures Alveolar macrophage	Cytotoxicity (via functional parameters) Carcinogenicity Neoplastic transformation DNA damage/repair
	Trachea	Cytotoxicity (via functional parameters) Carcinogenicity
	Liver	Carcinogenicity Mutagenicity (with/without metabolic activation) DNA repair/synthesis
	Lung	Functional/morphologic damage
	Ovarian/embryonic	Mutagenicity Toxicity Neoplastic transformation Chromosome aberrations DNA synthesis
	Endometrial	Co-carcinogenicity
	Lymphocytes	Mutagenicity Carcinogenicity
	Fibroblasts	Carcinogenicity Cytotoxicity Neoplastic transformation DNA damage/repair
	Epithelial	Carcinogenicity Enzyme kinetics
IN VIVO SCREENING	Fish (*Poecilia formosa*)	Carcinogenicity (*in vitro*/*in vivo*, clonal transplantation)
	Insects (*Drosophila melanogaster*)	Mutation
	Plant (*Tradescantia*)	DNA damage/repair (dominant, recessive lethals, chromosomal aberrations)
	Mammalian (Rodents)	Carcinogenicity (e.g., pulmonary) Mutagenicity (germ and somatic cells; dominant lethal, heritable translocations, point mutations) Teratogenicity (including exposure *in utero*) Chromosomal/morphological aberrations Immune system response (humoral and cell mediated) Toxicity (e.g., pulmonary) Combined *in vivo*/*in vitro* protocols (e.g., DNA repair, metabolites)
	(Primates)	Behavioral, CNS changes
	(Humans)	Changes in mutation rate (via antibody screens) Indicators of exposure (e.g., metals)

SUPPORT

- Procurement and characterization of test samples
- Chemical/biological availability of samples in *in vitro* test samples
- Environmental Mutagen Information Center (EMIC)/Environmental Teratology Information Center (ETIC)

mammalian cell lines, plants, insects, and mammals), a variety of end points (e.g., carcinogenic, mutagenic, and/or toxic responses) and assess a wide variety of biologically active agents, from pure substances to complex mixtures.

The bioscreening program comprises the first tier in a hierarchical testing sequence designed to evaluate the hazards associated with energy-related materials. The in vitro systems concentrate on the detection of biologically active agents, and, by utilizing a battery of tests, the sensitivity and selectivity of the testing sequence is improved (i.e., few false negatives). By incorporating redundant test systems, a wide range of pollutant classes can be examined. Cytotoxic, mutagenic and neoplastic transformations are considered as biological end points in both prokaryotic and eukaryotic cell systems. Since a substantial number of compounds require metabolic activation before a biological response becomes evident, the in vitro systems can utilize various microsomal enzyme preparations or host-mediated assay steps to mimic normal metabolic pathways, and, hence, can identify these active metabolites.

As the more biologically active compounds are identified with the rapid screen protocols, more definitive in vitro studies that provide quantitative dose-response information are instituted as the second tier in the testing hierarchy. These research efforts merge into the cellular toxicology program, which is discussed in detail in Section 4.0.

As the more hazardous compounds are identified, whole animal (*in vivo*) protocols are utilized to more clearly define the biological response in intact organisms (third tier). Since the *in vivo* experiments are relatively expensive and time consuming, compared to the *in vitro* systems, only those substances eliciting positive results in lower echelon tests are subsequently evaluated *in vivo*. The whole animal tests emphasize a quantitative risk assessment approach and provide an interface with the animal toxicological studies discussed in Section 5.0.

3.2 EXTENT OF PROGRAM

Since it has not proved economically feasible to separate and test directly the activity of each and every agent produced during a given fuel cycle, the bioscreening program is being utilized to detect the presence of biologically active components of the products, by-products, and residuals associated with various energy technologies. The main thrust of the program is directed toward those developing technologies of near and mid-term interest, mainly the coal-based energy cycle (conventional and advanced) and energy conserving technologies (e.g., wastes-as-fuel and conservation measures).

The bioscreening program focuses on several response indices by which to judge the biological activity of a particular sample; namely its carcinogenic, mutagenic, and toxic properties. In some instances, its biological activity may be implied, based on other testing results (e.g., mutagenic screening to identify suspect

carcinogens). Where appropriate, each of these response indices is evaluated by available *in vitro* and *in vivo* testing procedures. Research efforts are directed toward both complex (i.e., crude) pollutant mixtures and isolated fractions thereof, and generally progress from the *in vitro* screening protocols, to the more definitive *in vivo* procedures.

3.2.1 Carcinogenesis Screening

A variety of energy-related air pollutants are being tested for their carcinogenic potential in isolated test systems (i.e., *in vitro*). The carcinogenic activity of selected energy-related air pollutants is being evaluated using the CH3/10T 1/2 and BALB/c 3T3 neoplastic transformation bioassays. The sensitivity of the assay systems are improved by the inclusion of suitable metabolic activation systems and by the incorporation of biochemical indicators of carcinogenesis in addition to morphological transformation.

A variety of epithelial cell lines are being tested to determine the neoplastic transformation potential of specific pollutants. Since most human tumors are derived from epithelial tissues, these cell lines are highly relevant as screening tools.

Microbial tester strains (e.g., *Salmonella typhimurium*) are being utilized to implicate various materials as possible carcinogenic pollutant species. Compounds being tested include certain heavy metals, asbestiform particles, energy-related polycyclic hydrocarbons

(e.g., benzo(α)pyrene, dibenzofuran, 1,2,4-trimethyl-benzene, and methylbenzimidazole) and various other fractions of coal conversion or oil shale effluents.

The biological activity of agents obtained from coal and oil shale processes are being investigated for their ability to enhance carcinogenesis (i.e. co-carcinogens). The use of rodent cell lines in this bioassay system has indicated that the resultant DNA lesions are induced in a different manner than in human cell lines. Such findings indicate the need for caution in extrapolating research results from animal to human cell lines.

Whole animal (in vivo) carcinogenesis studies focus on pulmonary cancers resulting from air pollutants, alone and in various combinations (e.g., H_2SO_4 mists, particulate material, and polycyclic aromatic hydrocarbons). Pulmonary carcinogenesis studies involving BALB/c and C57B/6J mice strains are in progress. Since those strains have different incidences of spontaneous tumor formation, it is hoped that information can be obtained on the mechanisms of spontaneous tumor formation and on the interactive effects of pulmonary carcinogens on those strains (e.g., synergism, antagonism).

In order to assess the carcinogenic potential of energy related water pollutants on biota, a fish carcinogenic bioassay, utilizing the Amazon molly (Poecilia formosa), is being developed. Agents under test in this bioassay system include 7,12 dimethylbenz(α)-anthracene and its 5,6-oxide.

3.2.2 Mutagenesis Screening

The mutagenic potential of numerous crude and fractionated pollutants are being determined (and by implication, their carcinogenic behavior) using several microbial test systems (e.g., Salmonella typhimurium histidine deficient strains). Since studies have indicated that active metabolites of once suspected mutagenic agents are often the causal factors in positive test results, appropriate metabolic activation steps are being utilized, from direct addition of suitable enzyme preparations into the test medium to the testing of body fluids obtained from mammals previously exposed to the compound of interest. Further developmental work with the S. typhimurium system is underway using a number of derivatives of fluorene. Structure activity relationships, dose-response curves, and the bonding of these compounds or their metabolites to cells or macromolecules are being determined.

Selected mammalian cell lines (e.g., Chinese hamster ovary, Syrian hamster embryo, or mammalian lymphoid cells) are being utilized to detect point mutations resulting from exposure to selected energy-related pollutants. Mutagenic screening involving multiple loci tests and utilizing electrophoretic methods, is being developed to augment the existing mutagenic screening capabilities. The majority of materials currently under mutagenic test in isolated systems are crude and fractionated hydrocarbon samples generated by coal conversion or oil shale technologies.

In whole animal testing, more common air pollutants are also being evaluated for their mutagenic potential, alone and in various combinations. Specific loci tests in mice exposed to SO_2, benzo(α)-pyrene, and 7,12-dimethylbenz(α)anthracene are being conducted. More sensitive mouse strains are being developed to permit better multiple loci testing (via single and two dimensional electrophoretic techniques) than previously attainable. Studies are being conducted in mouse sperm cells to detect point mutational events using various enzyme systems as response indices.

3.2.3 Chromosomal/DNA Alterations

Chromosomal abberations in selected mammalian cell lines are being used to identify genotoxic effects of energy-related materials. Response indices include chromosomal breaks, chromatid exchanges, and non-disjunctions. Cell lines under test have been derived from the Chinese hamster, the Indian muntjac, and the deer mouse. This testing protocol is being extended to include human fibroblast and lymphocyte cell lines, thus becoming a valuable primary screening tool for effects upon human cellular material.

Additional studies include a comparison of polycyclic organic hydrocarbon effects on DNA synthesis in rat hepatocytes and the assessment of DNA damage using electrophoretic techniques. Pollutants under study include a selection of energy-related organics and heavy metals.

Genotoxic effects are being measured in mammals and plants (*in vivo*) exposed to various energy-related pollutants. Field studies are underway to evaluate the utility of *in situ* screening of the genotoxic effects of air pollutants on different varieties of spiderwort (Tradescantia).

3.2.4 Toxicological Screening

Both cellular and whole animal toxicity studies are being conducted on a number of energy-related pollutants. Cellular studies using alveolar macrophages are examining the toxic properties of particulate material, and selected metal ions. Response indices include cell viability, ATP content, functional integrity, and various enzyme activities. The effect of metallic oxide coated and uncoated fly ash on rabbit alveolar macrophages is currently being determined. Scanning electron microscopic examination is being conducted to map the elemental distribution within the cells.

Heavy metals (e.g., Pb, Cd) have been applied to cell cultures derived from nervous tissue, liver, and muscle. The effects of these metals on general growth, the induction of binding proteins, and the developmental expression of differentiated functions are being studied.

Whole animal studies stress pollutant exposure via inhalation, and include detailed studies of changes in lung structures and function resulting from pollutant exposures. Pollutants under

consideration include sulfur-containing compounds, NO_x, oxidants, metals, and selected hydrocarbons. As part of the overall program, biochemical indicators of pollutant exposures are being sought. A variety of laboratory techniques are under development that should be useful in defining the early, reversible, cytological changes in lung tissue following pollutant exposures (e.g., flow system analysis, cell separation, spin-labeling techniques).

In addition, a series of studies are underway to determine the influence of selected energy-related pollutants on whole animal immune systems, and in particular the respiratory immune system. By considering both cell-mediated and humoral immunities, as well as the developmental stages of each, the effects of pollutant exposures can be better understood.

3.2.5 Support Programs

Other research efforts include the development of combined testing protocols that allow an investigator to conduct a multitude of *in vitro* and *in vivo* experiments concurrently within a single animal testing sequence, thereby minimizing the resource investment substantially. A combined testing protocol is being developed to carry out the following studies in a single animal test: DNA repair in germinal and somatic cells, micronuclei test, metaphase analysis of bone marrow, spermatocyte tests, and analysis for active metabolites in blood and urine. Standard mutagens and environmental agents will be used to validate and calibrate the tests.

An extremely important support function is the establishment of a chemical repository for materials under test. Such a repository has been set up at Oak Ridge National Laboratory and receives, stores and disseminates specimens of energy related materials for testing.

Additional support is provided to the Environmental Mutagen Information Center (EMIC) and the Environmental Teratogen Information Center (ETIC), both computerized information retrieval systems containing current data describing the testing results of potentially mutagenic or teratogenic compounds.

3.3 PROGRAM UTILITY

The Interagency health effects R&D program has contributed, through the bioscreening effort, to the development, validation, and refinement of numerous *in vitro* and *in vivo* protocols to assess the biological activity of test samples. By incorporating this bioassay arsenal into a hierarchical approach, a methodology (utilizing *in vitro* and *in vivo* protocols) is available to rank on a priority basis the various energy-related pollutants, processes, or effluents. As more "real world" materials are assayed, appropriate reports describing energy processes in terms of the biological activity of their products, by-products, or residuals will be provided, so that more detailed health effects studies can be instituted as appropriate, or necessary control technology (process modification or post-combustion clean-up) can be applied. In so doing, a more efficient allocation of limited research resources can be focused on those high priority materials posing the greatest risk to human health.

3.4 RESEARCH NEEDS

Current research efforts have identified several areas that require resolution. Some of the *in vitro* protocols under development have been designed for their sensitivity toward specific types of biological responses (e.g., frameshift mutations or sensitivity toward polynuclear hydrocarbons) and require validation by *in vivo* testing. Current efforts to evaluate complex (crude) environmental samples often require extensive preparation prior to testing that can possibly affect the biological activity of the entire sample. Methods must be developed to permit existing bioassays to accept crude mixtures without prior purification.

Along with the above mentioned areas, the effects of various metabolic activation steps on the test results must be carefully defined. In certain instances, the simple inclusion of an activation control in experimental protocols has produced significant increases in biological response. The applicability of the chosen activation step to the organism in question must also be determined before any definitive answer can be found concerning the material's biological activity. Systems must be designed that are genetically and metabolically similar to man. More effort should be directed towards combined testing protocols, whereby parameters such as toxicity, DNA damage and repair, metabolism, mutagenesis, and carcinogenesis could be measured concurrently.

4.0 CELLULAR TOXICOLOGY

The cellular toxicology component of the health effects related Interagency Energy/Environment R&D Program is involved in the development and utilization of cell and tissue cultures to define the type and extent of biological activity associated with energy-related materials, to understand the mechanism of action of each agent, and to determine the cellular recovery and repair processes available. By monitoring a wider selection of biological end points than is available to the bioscreening effort, the cellular toxicology program is better able to determine the type and degree of damage sustained. Cellular research methods also permit more definitive pollutant exposures to selected tissues, since the physiological barriers normally encountered in whole animal studies are missing. In addition, cellular methods permit the evaluation of potentially toxic agents on cell systems in the absence of biological modifiers (e.g., hormonal influences). Cellular methods alone, however, cannot definitively assess pollutant damage, but should be used in concert with the bioscreening and animal toxicology efforts.

4.1 OVERVIEW

The cellular toxicology program can be divided into four major categories: the development of screening methods, early indicators of damage, damage and repair mechanisms, and fundamental research in cellular processes. The program is developmental in nature, supporting

the bioscreening and animal toxicology efforts, and utilizes pollutant samples of interest to those two programs.

The development of screening methods complements the bioscreening program by providing additional short-term cellular and molecular tests for mutagenesis, carcinogenesis, and system damage. Responses such as cell proliferation, differentiation, and changes in immuniological status or cell kinetics are being used to detect cytological reactions to environmental pollutants.

The objective of the second portion of the program is to develop useful early indicators of damage and methods for their application in routine monitoring. Cytological, physiological, and biochemical changes are indicative of early stages of damage, and may be useful as a means of detecting adverse effects before irreversible alterations occur.

The prevention of serious damage or dysfunction in an organism rests, in part, on the capability of cells to adapt to adverse conditions or to repair injuries. The third component of the cellular toxicology program attempts to define the basic mechanisms of pollutant interaction with key subcellular and molecular structures that are common to all species, and to define the repair processes for such damage.

Fundamental research efforts focus on an improved understanding of normal organ, tissue, and cell structure and function in order to better recognize damage. Membrane permeability, metabolic pathways,

enzyme activation, and the functional integrity of various cellular or organ systems are currently receiving emphasis.

4.2 EXTENT OF PROGRAM

4.2.1 Development of Screening Methods

The development of screening methods within the cellular toxicology program parallels efforts in the bioscreening program, since both utilize cell or tissue cultures in their research. The two programs are not duplicative, however, because the cellular toxicology effort is geared toward developing a basic understanding of biological systems (and thereby aiding in the selection of sensitive response indices), while the bioscreening effort applies these cellular and molecular systems to the actual identification of hazardous environmental agents.

The practical application of cellular testing systems often requires accompanying instrumentation development. A fast flow fluorometry technique is being perfected that is capable of not only handling large numbers of cells, but also sorting various classes of normal and damaged cells.

Organ, tissue, and cell cultures from those experimental animals currently used for *in vivo* dose-response studies are being developed (e.g., skin tissue cultures, tracheal rings). These cultures, having originated from the actual whole animal test species, permit a more detailed comparison between *in vivo* and *in vitro* results, than can be accomplished when the tissue cultures are not genetically similar to the whole animal. The development of human lymphocyte-lymphoblast

and fibroblast culture lines to assay for mutagenesis and oncogenic transformation is a valuable screening tool because of this ultimate genetic compatibility.

Work is underway to extend the lifetime of cell and tissue cultures and to shorten the time between pollutant exposure and observable response.

4.2.2 Early Indicators of Damage

The respiratory tract and skin receive major consideration in this portion of the program, since those systems are generally the prime routes by which humans are exposed to energy-related pollutants. Indicators of respiratory tract damage focus on the alveolar macrophage, because it represents the primary means of defense against inhaled materials, and lung epithelium, because of its rapid mitotic rate and proclivity to develop cancer.

Developments in the macrophage system include the addition of enzymatic, morphological, and functional indices of damage to the existing cell viability measurements. The ability to monitor the functional integrity of the alveolar macrophage is important, because of its involvement in lung clearance mechanisms.

Since lung epithelial cells demonstrate increased cell turnover in response to irritation, studies are underway to determine whether the turnover rate can be used as an indication of early damage and progression to latent disease, including cancer. Research efforts with skin and liver cell cultures are attempting to detect cytological and biochemical changes that correlate in time with the promotion and progression of cancer.

Research involving the gastrointestinal tract is aimed at detection of changes in absorption and excretion caused by toxic metals. While these studies have as their chief objective measurements of damage, they also involve work on retention and distribution of toxic metals in key organ systems.

4.2.3 Damage and Repair Mechanisms

A substantial effort is being directed toward evaluating the basic mechanisms of pollutant interaction at a cellular and subcellular level. At those levels, the mechanisms of damage may transcend mammalian species differences, and hence aid in extrapolation of information from experimental animals to man. Recent studies with carcinogenic polynuclear hydrocarbons indicate that exposure to those chemicals in the activated state result in DNA binding according to first order kinetics. Similar kinetics have been demonstrated for gene mutations and the initiation phase of carcinogenesis for several of the same hydrocarbons.

As a result of their sensitivity and proliferative activity, stem cells tend to magnify any injury experienced. Consequently, the immune and hematopoietic systems, both of which contain stem cells, have been suggested as good indices of pollutant toxicity. Both humoral and cell-mediated immunity are being examined after exposure to polynuclear hydrocarbons derived from coal gasification and oil shale technologies.

Although some progress has been made in studies of repair in procaryotic organisms, there is a need for more work in mammalian

cells, and especially human cells. Such work is just beginning and is hampered by the lack of repair-deficient mutants, except for cells derived from humans with xeroderma pigmentosum. Efforts are underway to select such mutants using novel methods.

4.2.4 Fundamental Research

Of major emphasis in the energy-related health effects program is the increased understanding of normal tissue and organ physiology, prerequisites for the assessment of damage resulting from pollutant exposures. The emphasis of the program is on developing a better understanding of the organ systems considered critical in terms of the route of entry upon exposure, or the need for rapid cell renewal to maintain system integrity.

Ongoing research relates to biochemical and functional aspects of lung surface cells and membranes, since they usually represent the initial site of pollutant exposure. Lung membranes are being subjected to a variety of air pollutants (e.g., SO_2, NO_2, hydrocarbons, O_3) alone and in combination, and various functional or biochemical indices monitored (e.g., enzyme activity, lipid metabolism, binding capacity).

The hematopoietic and immune systems are suspect as critical because of the potential sensitivity of the stem cell populations. Efforts are underway to culture hematopoietic stem cells in semi-permeable membrane chambers and fractionate and sort various types of leukocytes based on shape, size, and biochemical and immune function. Efforts are devoted to understanding the molecular mechanisms which

regulate differentiation of various classes of leukocytes and the factors which interface with the regulation of diseases, including leukemia.

4.3 PROGRAM UTILITY

The cellular toxicology program is developmental in nature, and provides systems, methods, and instrumentation for application within the other segments of the Interagency R&D Program. The biological screening effort receives not only systems development support, but also guidance in the elucidation of early indicators of damage. With a better understanding of normal cell or organ physiology, the identification of target organs in whole animal experimentation is improved. Fundamental research can provide information on cellular systems that span a multitude of species, and hence aid in efforts to extrapolate animal data to man. By elucidating the mechanism of toxic action of energy-related compounds under test, a better understanding of basic biological concepts is developed.

4.4 RESEARCH NEEDS

It becomes difficult to define specific research needs in the area of cellular toxicology, because only by complete understanding of the normal physiological and biochemical processes can one insure valid interpretation of pollutant impact in these areas. However, increased research emphasis in selected areas will be most beneficial. Improved understanding of pharmacokinetic and toxication/intoxication mechanisms is crucial to the prediction of potential hazards of energy related pollutants. Non-destructive indicators of impaired physiological

function in whole animals would be a welcome addition to the testing arsenal. Improved cell culture techniques that increase the useful lifetime of the culture would be beneficial to the research program. The expanded use of cell lines derived from humans in a variety of testing protocols would greatly improve the extrapolation potential of cell and tissue culture techniques.

5.0 ANIMAL TOXICOLOGY

Animal toxicological studies, by reducing the uncertainties in the estimates of the quantitative dose-response relationships between pollutant exposure and effect, assist in providing the capabilities to evaluate short- and long-term hazards to man (normal, susceptible, and stressed populations) from simultaneous exposures to combinations of stresses primarily associated with energy technologies. The use of whole animal toxicological tests offers several advantages for assessing the biological activity of potentially hazardous compounds. Whole animal toxicity tests can be performed relatively quickly and inexpensively, when compared to clinical human health studies. Experimentation protocols, including exposure conditions, are also more easily maintained. Inherent in the use of whole animal systems to test toxic materials is the consideration of the metabolism and fate of the compound under test. The judicious choice of animal species has been shown to provide a reasonable estimate of probable human response to the toxic agents. In addition, the use of whole animal toxicological testing to define potential human health impacts is needed because of the lack of previous human exposures (especially with the developing energy technologies) and the ethical restrictions associated with experimental exposure of human volunteers to toxic materials.

The Interagency health effects related R&D program involves not only the actual testing of hazardous materials to establish dose-response relationships (under a variety of exposure conditions) but also the identification of particular animal strains which, based on their sensitivity to selected pollutants, can be used to model those human organs, systems, or individuals which are most susceptible to that particular stress. The emphasis of the animal toxicology program is on developing dose-response relationships for adverse pulmonary effects (e.g., dysfunction, carcinogenesis) caused by air pollutants from coal conversion or combustion and near term energy conservation technologies.

5.1 OVERVIEW

That portion of the Interagency health effects-related R&D program involving animal toxicological studies can be described in terms of the health end points under investigation, the target organs or systems under scrutiny, or the pollutants of concern (see Table 5-1). The program is intended to provide quantitative data describing pollutant effects on whole animal systems (*in vivo*) to complement those areas where bioscreening or cellular toxicology efforts are ineffective or unreliable. *In vivo* studies defining the long-term, low-level pollutant effects from single and multiple exposure pathways (e.g., inhalation/ingestion) are progressing. However, whole animal studies, since they are expensive and time-consuming to conduct, rely on bioscreening efforts to identify those pollutants representing high

TABLE 5-1 ANIMAL TOXICOLOGY TEST PROGRAM

HEALTH END POINTS	TARGET ORGANS/SYSTEMS
Carcinogenicity	Pulmonary
Mutagenicity	Cardiovascular
Teratogenicity	Reproductive
Toxicity	Central Nervous System (CNS)
Physiological Damage (e.g., deposition/retention, functional capacity, metabolic or biochemical changes)	Immune
	Various Isolated Organs (e.g., liver, kidney, brain)

AGENTS OF CONCERN

Aerosols (including fibrous amphiboles and secondary formation products)

Criteria Pollutants (i.e., SO_x, NO_x, Oxidants, Suspended Particulate Matter, Hydrocarbons, and Carbon Monoxide and their atmospheric derivatives

Electromagnetic and Corpuscular Radiation (ionizing and non-ionizing)

Organic Compounds (esp. polynuclear aromatic hydrocarbons)

Trace Metals (e.g., Pb, Cd)

priority hazards requiring extensive in vivo testing. The program also addresses those non-lethal effects of pollutant exposures that reduce an organism's life-span, or produce decrements of functional activity in a particular system of sufficient magnitude to make the host more susceptible to damage from other stresses.

A large portion of the animal toxicology program is devoted to the elucidation of various pollutants' effects on mammalian pulmonary systems under a variety of exposure conditions. Physiological damage resulting from localized deposition and/or retention of pollutants, a loss of functional integrity in the entire system, a reduction in auto-immune response capacity, and various metabolic and biochemical changes are being considered. To a large extent, the program addresses the impacts on pulmonary function of criteria pollutants (including their atmospheric reaction products) and in particular SO_x, NO_x, and respirable particles. Parametric studies are underway to define the interrelationships between pollutant combinations that can result in significant interactive effects (e.g., synergism).

Reproductive, CNS, and immune system response to various pollutant exposures (including electro-magnetic and corpuscular radiation) are being evaluated in whole animal studies, since current in vitro techniques are unable to do so. In vivo germinal cell studies (mutagenic potential, viability) and teratogeny studies for a number of pollutants including SO_2, selected polynuclear aromatic hydrocarbons, and tritium are underway, as are studies to define CNS

effects from trace metal exposures, organic compounds, and non-ionizing electromagnetic radiation. Immune system response (in particular, pulmonary immune systems) to pollutant stresses are being defined so that indirect effects on whole animal infectivity resulting from pollutant exposures can be determined.

5.2 EXTENT OF PROGRAM

The animal toxicology program focuses primarily on pollutants released during the coal fuel cycle, especially during combustion and/or conversion, and to a lesser extent on pollutants resulting from energy conservation activities. Many of the pollutants under study are generic, in that they may be a result of other energy technologies and other industries as well (e.g., organic compounds, trace metals, sulfur-containing compounds). The program is oriented toward defining dose-response phenomena resulting from inhalation exposures, since this represents the primary route of exposure to environmental pollutants for a majority of the population. However, the program does not neglect other routes of exposure (e.g., ingestion, dermal absorption) since some have been shown to result in significant pollutant accumulation in the body under certain exposure conditions. The relative contribution of multiple exposure routes (e.g., inhalation/ingestion) to an individual's total body burden is currently receiving greater attention than in the past.

EPA, ERDA, and NIEHS make major contributions to the animal toxicology program, with each reflecting their respective missions. EPA is heavily involved in defining animal dose-response relationships for numerous air pollutants to provide support for their regulatory activities. Definitive dose-response information describing the adverse health impacts of criteria and non-criteria air pollutants are being developed in close cooperation with existing EPA programs supported by base budget funds. Of special interest are the respiratory effects arising from low-level, intermittent exposures to fossil fuel combustion products. Preliminary results indicate such effects on lung metabolism are reversible, but the long-term biological significance of such exposures remains undefined.

EPA is also examining the carcinogenic activity of certain non-organic energy-related pollutants and is focusing efforts on the impacts of trace metals and mineral fibers on mammalian respiratory systems. Emphasis is also given to efforts describing the effects of multiple pollutant exposures, so that the role of cofactors or promoting agents can be more clearly defined. The EPA program is aimed at obtaining data that will be useful for the application of pollutant control measures and the setting of suitable emission standards for both criteria and non-criteria pollutants.

ERDA participation in the animal toxicology effort emphasizes the detection of carcinogenic materials that are present in coal conversion or oil shale-related activities. After interpreting

the carcinogenic activity of those complex samples, quantitative comparisons are being made between selected fractions of the crude materials. Dermal applications, inhalation, and intratracheal exposures are being examined. In cooperation with ERDA, EPA is incorporating in vivo systems to quantify those potential hazards associated with emerging energy technologies, so that pollution abatement or control activities can be initiated during the development stages of a particular engineering process, rather than as an expensive retrofit application.

The NIEHS portion of the research program provides basic support, mainly in the areas of target organ toxicity, effects on germinal cell development (e.g., oogenesis, spermatogenesis), teratologic studies and inhalation modelling. Metabolic studies, using isotopically labeled hydrocarbons and their metabolites, are being conducted. The NIEHS program is intended to provide basic research support which will ultimately contribute better toxicological procedures with which to evaluate the potential hazards associated with energy technologies.

5.3 PROGRAM UTILITY

The whole animal testing program provides several direct and indirect benefits. By coupling the animal testing program with the bioscreening and cellular toxicology efforts, a comprehensive hierarchial basis is developed for predictions of adverse human health impacts from energy related pollutants. As more definitive

dose-response relationships are developed in whole animal systems, technology development as well as regulatory activities can concentrate their efforts as needed. Documentation addressing pollutant specific, process specific, or biological testing protocols will be developed as appropriate.

In addition to the primary benefits of the program, several secondary benefits arise. The bioscreening program provides data to direct any subsequent whole animal testing, and in return receives information that is used in the validation of the bioassay testing protocols themselves. This program, therefore, offers a unique opportunity to match the *in vitro* screening and conventional whole-animal protocols by performing controlled correlative tests on identical crude materials and chemicals. In addition, whole animal studies provide insight into target organ toxicities for use in the cellular toxicology program.

5.4 RESEARCH NEEDS

Although there is a noteworthy effort using whole animal studies (coupled with *in vitro* programs) to define the hazards associated with pollutant exposures, several areas have been singled out as requiring more emphasis. There is an urgent need to have available more testing methods that reliably indicate slight organ or system dysfunction prior to the onset of irreversible damage. The effects of energy related pollutants on the reproductive function of populations chronically exposed at low levels must be clearly defined.

Current interest focuses on gross indications of reproductive damage (e.g., birth defects), but must also address the less evident impacts on population fertility and fecundity. In addition, the possible interactive effects from multiple pollutant exposures must be better defined, and should not be restricted to combinations of only energy-related pollutants or sources. Further work to specify toxicologic manifestations of inhalation exposures, especially in stressed or susceptible populations, is needed, as is better definition of multiple exposure pathways in relation to the total body burden concept.

6.0 HUMAN HEALTH STUDIES

The health effects-related Interagency Energy/Environment R&D Program provides support to study human health effects resulting from exposure to energy-related pollutants or activities. In general, this program has been formulated to (1) identify specific pollutants and characterize their effect on human health, (2) study normal, susceptible, and stressed human populations in order to determine their response sensitivity to various pollutants, and (3) define the hazards associated with those pollutant exposures in occupational groups or the general public. In the final analysis, such information will be utilized in developing suitable regulatory policies and identifying those new energy-producing technologies having fewest threats to public health. The classes of pollutants addressed in the energy-related research are those which are most frequently emitted from fossil fuel-fired sources, namely sulfur oxides (SO_x), nitrogen oxides (NO_x), organics and particulate material.

6.1 OVERVIEW

Basic toxicological and epidemiological studies, as well as clinical research involving human subjects, all play important roles in this segment of the R&D effort. Toxicological research focuses on the development of methodologies that can be utilized to assess the adverse effects of energy-related materials in humans. Whereas it is recognized that animal and cellular oriented

studies are of distinct value in assessing the harmful effects of environmental pollutants, the limitations in applying such research to humans is apparent. It is expedient to utilize animal systems, but differences in species response to different agents must be considered.

Epidemiological research is involved with the determination of relationships between human health impact and pollutant exposures. The application of valid statistical and data gathering techniques in the conduct of these population studies is extremely important. Since most adverse health impacts linked to pollutants are a result of chronic, low-level, often intermittent exposures, dose-effect associations are extremely difficult to establish. Although a majority of the epidemiological component is concerned with general population studies, some effort is also directed toward investigating energy-related hazards from an occupational health perspective.

Clinical studies examine the pathological evidence in human subjects exposed, mainly at low levels, to the major pollutants of interest (e.g., sulfates, H_2SO_4 mists, particulate material). Sophisticated clinical measurements defining the health effect, coupled with detailed characterization of the pollutant exposure profile, provide direct evidence of the causal relationships between pollutant exposure and effect.

6.2 EXTENT OF PROGRAM

6.2.1 Clinical and Toxicological Research

Because of the grey area dividing these two studies and because many projects combine diagnosis and treatment with experimental procedures, clinical and toxicological studies are discussed together. The Clinical Laboratory Evaluation and Assessment of Noxious Substances (CLEANS) project forms the nucleus of EPA clinical studies and provides the Controlled Environmental Laboratories (CELs), which simulate a variety of polluted atmospheres.

In the CELs, human subjects are exposed for extended periods of time to pollution levels similar to those found in urban areas or areas adjacent to energy-related facilities. The CLEANS laboratories allow researchers to perform experiments addressing a wide range of physiological responses. Especially important in each CEL are the instruments to measure the functioning of heart and lungs before, during, and after exercise. In addition to the evaluation of cardiopulmonary status, studies of immune mechanisms, hematologic and metabolic parameters, and neurobehavioral functions are being conducted with these subjects.

Studies focus on pollutants that result directly or indirectly from fossil fuel combustion. Current efforts include the clinical assessments of sulfuric acid aerosols, ammonium sulfate and bisulfate, various nitrates, ozone, and particulate material. A wide range of exposure profiles are being assessed, including a variety of pollutant combinations, mass concentrations, and droplet sizes.

Also part of the research program are efforts to compare clinical signs of pollutant effects in normal and susceptible human subjects. Persons suffering from respiratory problems (e.g., asthma, bronchitis), smokers, and children or the elderly, tend to be effected to a greater degree than the average population. Studies of this kind are necessary to properly assess the "margin-of-safety" currently used in regulatory standards.

6.2.2 Epidemiological Studies

Population studies currently address the health impacts associated with exposure to energy-related pollutants via inhalation or ingestion. The effects of ingesting water containing trace metals or organic pollutants associated with energy facilities are being determined. Several studies are underway to define the health impacts associated with heavy metal ingestion, by using metal concentrations in biological tissues (e.g., teeth, hair) as indicators of exposure.

The morbidity and mortality of populations exposed to pollution from coal combustion or conversion are being compared to that of the general populace. In association with the Tennessee Valley Authority and NIOSH, clinical and epidemiological studies are being conducted to investigate pulmonary disease and neoplasia in workers employed at coal-fired steam electric generating plants.

Being involved in large scale epidemiological studies, the EPA is supporting the Community Health Air Monitoring Program (CHAMP), which monitors continuously at selected sites for a number of air pollutants (e.g., SO_2, NO_2, O_3, suspended particles). This monitoring

effort is essential to a comprehensive epidemiological program, because accurate exposure profiles are an integral part of the effort.

Several occupational epidemiological studies, in addition to the TVA effort mentioned previously, are underway. Effects of environmental conditions in Alaskan pipeline workers are being evaluated, and various work practices assessed (e.g., work-rest regimen, fluid and food intake, clothing, and heating devices). Another study is defining the hazards to divers involved in offshore oil development. A third study focuses on the hazards associated with employment in the mineral, wool, and clay fiber production industry.

6.3 PROGRAM UTILITY

The Interagency Program's human health studies conducted by the four participating agencies should be considered complementary to their existing base budget-supported efforts. Recent expansion of the analytical and clinical capabilities with EPA's CLEANS effort is an example that will have wide-spread impact on ongoing and proposed clinical and epidemiological studies. The development of specific information transfer capabilities (e.g., EMIC, ETIC) provides for the rapid and accurate disbursement of scientific information so needed in the rapidly expanding energy/environment field.

A substantial effort of the Interagency health-related R&D Program has been toward identifying and quantifying human health risks through the use of *in vitro* and *in vivo* toxicological methods. The human health studies program is intended to augment those research activities by confirming their findings in human systems, and by

providing a more definitive basis for cost/risk/benefit analyses that are often required for regulatory action.

Since clinical and epidemiological health studies require large investments of time and resources, it is imperative that no unnecessary duplication of effort exists. The Interagency Program has been designed to complement existing base programs for those agencies involved. Many of the empirical results will eventually be utilized by scientific disciplines divorced from the Interagency Energy/ Environment R&D Program.

6.4 RESEARCH NEEDS

The work that is outlined above, although evidence of the significant progress in the detection and evaluation of pollutants from energy sources on human health, illustrates the need for expanded research. Among the areas requiring expansion are data sources such as ETIC and EMIC to provide a maximum information base. In addition, more emphasis on systems for reporting pathological manisfestations and for monitoring human populations for mutations, cancers, and terata is desirable. The interactions of multiple pollutants, as well as dose-effect relationships, are an essential aspect of human health hazards that need more intensive investigation. Epidemiological studies of a retrospective and prospective nature must be set up for pollutants shown to be hazards by clinical, animal or cellular methods. Procedures for such studies must be designed to assure acceptibility of the results.

7.0 RISK ASSESSMENT/DATA EXTRAPOLATION

The aim of the risk/assessment/data extrapolation effort is to provide a reasonable estimate of the risk to which an individual or population is subjected as a result of exposure to a hazardous pollutant. Since pertinent human data are rarely available, increasingly greater reliance is being placed on the extrapolation of human risk factors from animal experimentation. In estimating human risk from data generated in the laboratory, two problems must be recognized. More often than not, high dose levels and dose rates are used in the laboratory to elicit rapid and marked response; these high dose levels are not necessarily representative of the low environmental levels to which man is exposed. One also must acknowledge the second problem; namely, the difficulties of converting estimates of risk for animals to corresponding estimates of risk for man.

7.1 OVERVIEW

The development of theoretical models to provide estimates of health hazards to humans may be classified into two general areas: (1) low-dose extrapolation; and (2) species-to-species comparison. Mathematical models to determine time from pollutant exposure to tumor occurrence, for example, have been generated for low-dose extrapolations. However, the validity of a model can be questioned if the assumptions upon which it is based are not met. If the length

of exposure is not indicative of the total dosage received (possibly due to inherent variations in metabolism) then the extrapolation can yield erroneous results.

Difficulties in extrapolation from animal data to humans may occur due to species differences in metabolism, absorption, or excretion, among others. Whereas adjustments have been made to create dose equivalents (e.g., grams/unit body weight or surface area), simplified solutions are not generally applicable when dealing with human risk assessment.

7.2 EXTENT OF PROGRAM

Several methods have been employed in the risk assessment/data extrapolation effort in order to define the incremental risk from pollutant exposures. Selected panels of experts have been utilized, as circumstances required, to review and evaluate the data and make risk assessments based on scientific judgment. In addition, the development and utilization of statistical models to predict the risks from exposure to noxious substances have become a substantial part of the R&D effort. These models include low dose extrapolations, species-to-species comparisons, and direct risk assessment methodologies.

7.2.1 Low-Dose Extrapolations

A statistical model has been developed to predict the risks associated with continuous exposure to a direct-acting carcinogen (i.e., a carcinogen affecting cellular DNA directly) at low,

environmental levels by using high dose level animal data. The model is general enough to reflect both linear responses associated with the one-hit model, as well as the non-linear responses reflecting probabilistic multi-stage events.

Computer simulation models have been developed to predict physiological responses to pollutant exposures by taking into consideration the metabolism and kinetics in a constant environment. Models are also being developed for assessing health impacts from changing levels of air pollution. The linear non-threshold model is considered appropriate for a number of carcinogens; however, a major problem that remains is the determination of a suitable slope for the linear dose-response model.

7.2.2 Species-to-Species Comparisons

Efforts involving species-to-species comparisons have emphasized carcinogenesis as a response index. A compilation of published carcinogenesis information is being prepared, which contains data that can be used to establish dose equivalency between species, metabolic activation/detoxification factors, and inter- and intra-species dose-response relationships.

Research is being pursued that gives insight into chronic and acute exposure effects, adaptation processes, and indices useful for identifying sublethal damage. In line with the emphasis on respiratory tract pollutants, models are being developed to describe the deposition characteristics, geometrical features, and kinetics of the

respiratory passages of laboratory rodents, dogs, monkeys, and humans. The observed relationships should offer a gauge as to the extent that results of subsequent experiments in those mammalian species can be extrapolated to man.

In addition, the comprehensive environmental mutagen and teratoge: information systems (EMIC, ETIC), discussed previously, provide a means by which species differences in response to a multiplicity of stresses can be methodically determined.

7.2.3 Direct Risk Assessment Methodologies

Efforts are being directed toward developing novel statistical methodologies that can function effectively with very small sample sizes, so that when minimal human health effects data are available, they can be efficiently used (e.g., epidemiological studies on small occupationally exposed populations). In addition, risk estimation is being performed by *ad hoc* groups of experts who review available data, deduce dose-response relationships (and associated uncertainties), and develop best estimates of the risks from exposure to a number of biologically active compounds.

7.3 PROGRAM UTILITY

The output from the risk assessment/data extrapolation effort can be used not only in regulatory decisions, but also in a wide variety of studies requiring data comparisons and extrapolations (e.g., development of priorities). The models that are developed, as well as the methodologies used in their development, will provide

useful tools for risk assessments in areas other than energy technology.

7.4 RESEARCH NEEDS

Additional effort must be directed toward utilizing limited *in vitro* and *in vivo* (rodent) studies to estimate human health risk, since only in a small number of cases will an extensive human data base exist. The effects of genetic variability within human or animal populations requires definition, especially as they impact the arbitrary "margin-of-safety" concept currently in vogue with standard-setting practices. The reliability of the various extrapolation models must be defined, especially when inherent assumptions cannot be easily met.

Appendix

A compilation of all research projects supported by the Interagency health-related Energy/Environment R&D Program since its inception is provided in Table A-1. In examining the available information pertaining to each project, a list of descriptive components was developed so that pertinent data relating to each project could be presented in matrix form. Each health effects research project supported by the Interagency Energy/Environment R&D Program is described according to the following:

- Project title
- Participating agency (i.e., EPA, ERDA, NIEHS, NIOSH)
- Project officer and program coordinator
- Principal investigator and affiliation
- Planned period of performance
- King-Muir sub-objective(s) as defined by Table A-2
- Applicable discipline - (i.e., bioscreening, cellular toxicology, animal toxicology, human health studies and risk/assessment/data extrapolation)
- Health end point
- Routes of administration
- Target or tissue of concern
- Agent (pollutant) characteristics
- Environmental medium in which that agent may be found
- Applicable energy technology producing that agent of concern

It should be recognized that these research projects represent the program since its inception and not just the projects currently supported. Table A-1 is based on information describing these

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projects as found in appropriate project progress reports, SSIE documents, and annual project or program status reports. Numbers assigned to the projects are only intended to provide a rapid reference capability within this document. The general arrangement of projects progress from King-Muir objective area #1 to objective area #5 (see column 6). The objective area listed first for a project provides the primary classification (as defined in the available documentation). When a research project contained aspects pertinent to other K-M classifications, it was so noted. As can be seen in Table A-1, there are numerous examples of research projects that could be appropriately classified into a number of K-M categories.

Those ERDA projects that were initiated under the auspices of the Interagency Energy Environment R&D Program in FY 75, but subsequently supported by ERDA's base budget are so noted.

Table A-2 provides a detailed listing of the five King-Muir objective areas and their subordinate headings.

CT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE†	DISCIPLINE APPROACHES	HEALTH END POINT
ical Characterization and Biological Effects tal Binding Agents Present in Emissions from le and Stationary Sources	EPA	Lee/Campbell (Cincinnati)	Finnelli, University of Cincinnati	6/74 - 6/77	1A4, 3B1, 2B2, 4B3, 4B2	Bioscreening	Cytotoxic
rmination of the Influence of Mineral Co-ors in Conjunction with Carcinogens from gy Related Materials	EPA	Coffin (RTP)	Palekar, Northrop Services	12/75 - --	1A1, 4C1	Bioscreening	Carcinoge cocarcino
toxicity Evaluation of Selected Sulfates and of rce and Ambient Air Samples	EPA	Huisingh (RTP)	Campbell, Northrop Services	-/74 - 9/76	1A4, 1A1	Bioscreening	Cytotoxic
lementation of Screening Tests for Potentially rdous Airborne Particulate Materials Using the olar Macrophage Test System	EPA	Waters/ Huisingh (RTP)	Campbell, Northrop Services	12/76 - /76	1A4	Bioscreening	Cytotoxic
are Pulmonary Carcinogenicity of Known Carcinogens and without Added Airborne Particles and Evaluate Influence of Added Gases and SO_4 Mists	EPA	Coffin (RTP)	Laskin, New York University	7/75 - 8/77	1A1	Bioscreening	Carcinoge
elopment of Methods for Determination of Carcino-esis by Bacterial Mutagenesis Employing Crude erial from Alternate Energy Sources	EPA	Coffin (RTP)	Commoner, Washington University	-/75 - --	1A1, 1A2	Bioscreening, methods development	Mutagenes sumptive genesis
elopment and Application of Automated Screening hodology for Evaluating Modification Candidate lutants of Patterned Behavior in Pri	EPA	Reiter (RTP)	Buck, Iowa State University	-/75 - 7/78	1A4	Bioscreening, methods development	Behavior cation
curement and Characterization of Refin cles	EPA	Kirtz (RTP)	Knudson, Illinois Institute of Technology Research Institute	7/75 - 9/76	1A4, 2A2, 2A3	Bioscreening	Support
vitro Screening of Selected Air Pollutants f ential Carcinogenicity Using Microbial System	EPA	Waters (RTP)	Research Triangle Institute	1/77 - --	1A1, 1A2	Bioscreening	Carcinoge
vitro Screening of Selected Air Pollutants for ential Carcinogenicity Detection of Genotoxic ects of Environmental Chemicals in Cultured er Cells	EPA	Huisingh (RTP)	Williams, American Health Association	9/76 - 8/79	1A1	Bioscreening, method development	Carcinoge
bined Mutagenic Protocol for Detecting Environ-tal Mutagenic Agents		Stara (Cincinnati)	Legator, University of Texas, Galveston	8/76 - 8/78	1A2, 2B1, 2B2	Animal toxicology, bioscreening	Mutagenes
ntitative Mutagenesis Testing in Mammalian llular Systems	ER	Stapleton (ERDA)	Hatch, Lawrence Livermore Labortory	--	1A2, 3A1, 5A2	Bioscreening	Mutagenes
phological Variants in Damaged Sperm	ERDA	Stapleton (ERDA)	Wyrobek, Lawrence Livermore Laboratory	--	1A1, 1A2, 1A3, 3B1, 3B3, 5A1	Bioscreening	Mutagene carcinog teratog
teriophage System for Screening for Carcinogeni-y of Polycyclic Aromatic Hydrocarbons	ERDA	Stapleton (ERDA)	Weiss, Franklin McLean Memorial Research Institute - University of Chicago	5/75 - 5/77	1A1, 1A2	Bioscreening	Carcinog mutagene

† K-M Objective, subheading, task; see Table A-2 for key.

	K/M SUB-OBJECTIVE[†]	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
17	1A4, 3B1, 2B2, 4B3, 4B2	Bioscreening	Cytotoxicity	In growth media	Enzymes	Particles (heavy metals), sulfates, CO	Air	Fossil fuel, automotive
	1A1, 4C1	Bioscreening	Carcinogenesis, cocarcinogenesis	Intratracheal instillation, intrapleural innoculation	Plumonary, pleural rabbit alveolar macrophage and red blood cells, mice, hamsters, rats	Fibrous amphiboles, polycyclic hydrocarbons, asbestos	Air	Coal (g[a],l[b]) oil shale
5	1A4, 1A1	Bioscreening	Cytotoxicity	In growth media	Rabbit alveolar macrophage, human lung fibroblast	Sulfate, chloride salts [e.g., Zn, Mn, Ni, Cu, Cd, Hg, Se, V], $Zn(NH_4)_2$, $ZnSO_4 \cdot 6H_2O$ particles	Air	Fossil fuel
76	1A4	Bioscreening	Cytotoxicity	In growth media	Alveolar macrophage	Particles (standard and crude)	Air	GA[c]
7	1A1	Bioscreening	Carcinogenicity	Inhalation, intubation	Golden hamsters	Benzo(a)pyrene (BaP), H_2SO_4 mists, trace metals	Air	Fossil fuel
	1A1, 1A2	Bioscreening, methods development	Mutagenesis/presumptive carcinogenesis	In growth media	Salmonella typhimurium, enzymes	Crude and fractionated materials, physiological metabolites	Multi	GA
8	1A4	Bioscreening, methods development	Behavior modification	Inhalation	Primates, CNS	Crude materials	Air	Coal (g, l)
5	1A4, 2A2, 2A3	Bioscreening	Support	N/A[d]	N/A	Particles (metal oxides, asbestiform)	Air	Fossil fuel
	1A1, 1A2	Bioscreening	Carcinogenicity	In growth media	S. typhimurium	Particles, vapor	Air	GA
9	1A1	Bioscreening, method development	Carcinogenicity	In growth media	Liver cell system, S. typhimurium	Environmental chemicals	Air	GA
8	1A2, 2B1, 2B2	Animal toxicology, bioscreening	Mutagenesis	Injection, ingestion	Microbial mutagenic screen, mouse	Environmental mutagenic agents	Multi	GA
	1A2, 3A1, 5A2	Bioscreening	Mutagenesis	Tissue culture, in vivo	Chinese hamster ovary, Syrian hamster embryo, yeast (S. cerevisceae)	Multiple pollutants	Multi	Coal, oil shale
	1A1, 1A2, 1A3, 3B1, 3B3, 5A1	Bioscreening	Mutagenesis, carcinogenesis, teratogenesis	Multi	Sperm (mouse)	Multiple pollutants	Multi	Coal, oil shale
7	1A1, 1A2	Bioscreening	Carcinogenesis, mutagenesis	Bacterial media application	Bacteriophage	Polycyclic aromatic hydrocarbons (PAH)	Multi	GA

[†] K-M Objective, subheading, task; see Table A-2 for key.

[d] Not applicable

[a] gasification

[b] liquefaction

[c] Generally Applicable

TABLE A-1
INTERAGENCY HEALTH EFFECTS R&D PROGRAM
PROJECT/RESEARCH PARAMETER MATRIX

	PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	EN
5	Pulmonary Carcinogenesis Test System	ERDA	Stapleton (ERDA)	Try, Argonne National Laboratory	--	1A1	Bioscreening	Carci
6	In-vitro Screening Assay for Cocarcinogenic Agents Produced During Coal and Oil Shale Processing	ERDA	Stapleton (ERDA)	Byfield, UCLA Laboratory of Nuclear Medicine and Radiation Biology	--	1A1, 1A4	Bioscreening	Cocar
7	Detection of Early Changes in Lung Cell Cytology by Fast Flow System Analysis	ERDA	Stapleton (ERDA)	Steinkamp, Los Alamos Scientific Laboratory	--	1A4, 2B1	Bioscreening, cellular toxicology	Cytot
8	Analysis of Effects of Energy Related Toxic Agents in Karyotype Stability in Mammalian Cells	ERDA	Stapleton (ERDA)	Deaven, Los Alamos Scientific Laboratory	--	1A4, 1A1, 1A2	Animal toxicology	Cytot
9	Rapid Assay for Carcinogenic Potential of Coal Conversion By-Products*	ERDA	Stapleton (ERDA)	Yuhas, Oak Ridge National Laboratory	1/76 - 7/77	1A1	Animal toxicology	Carci
10	Mutagenicity Assay of Fractionated Coal-Conversion Products	ERDA	Stapleton (ERDA)	Epler, Oak Ridge National Laboratory	--	1A2	Bioscreening	Mutag
11	In-vivo Screening for Gene Mutations in Mouse Germ Cells and Somatic Cells	ERDA	Stapleton (ERDA)	Russell, Oak Ridge National Laboratory	--	1A2, 4C2	Bioscreening	Mutag
12	In-vitro Chemical Cocarcinogenesis of Hormones and Polycyclic Aromatic Hydrocarbons	ERDA	Stapleton (ERDA)	Gerschenson, UCLA Laboratory of Nuclear Medicine and Radiation Biology	--	1A1, 1A4, 2B1, 5A1	Cellular toxicology	Cocar
13	Chemical Induction of Chromosome Aberrations in Mouse Germ Cells by Coal Conversion Products (Metals and Hydrocarbons)	ERDA	Stapleton (ERDA)	Generoso, Oak Ridge National Laboratory	--	1A4, 4B2, 1A2	Cellular toxicology	Bioch chang
24	The Effects of Cadmium on the Ultrastructure of Type A Spermatogonia	EPA	Stara (Cincinnati)	Jordan, Grambling College	8/74 - 7/76	2B1	Animal toxicology	Toxic
25	Biochemical Effects of Energy Consumption Related Trace Metals (Cd, Hg, Ni, As, Pd, Pt) on Pulmonary Macromolecular Metabolism	EPA	Lee (Cincinnati)	Bhatnagar, University of California, San Francisco	6/74 - 6/78	2B1, 2B2, 2B3	Cellular toxicology, animal toxicology	Toxic
26	Development of Cellular Model System to Determine Cytotoxicity from Alternate Energy Sources	EPA	Waters (RTP)	Bowers, Rockefeller	11/75 - 8/79	2B1, 1A4, 5B1	Bioscreening	Cytot
27	Development of Bioindicators of SO_2/NO_2 Exposure	EPA	Bruce (RTP)	Bollinger, Southwest Foundation for Research & Education	-/75 - 2/79	2B2	Human health studies	Toxic
28	Development of Physiological and/or Biochemical Indicators for Use in Epidemiologic Studies	EPA	Hayes (RTP)	not yet awarded	-/78 - --	2B2, 2B3	Human health studies	Toxic epide
29	Enzymatic Characterization of Metabolic Activation Potential and Identification of Presumptive Carcinogen Metabolites in Isolated Test Systems	EPA	Huisingh (RTP)	Weinstein, Columbia University	6/77 - -/80	2B2, 1A1, 3B3	Bioscreening, methods development	Carci
30	Application of Automated Behavioral Testing System to Monkeys Exposed to Coal Conversion Pollutants	EPA	Reiter (RTP)	not yet awarded	-/77 - --	2B3	Bioscreening	Behav ficat
31	Workshop on "Screening Systems for Alternate Energy Effluents"	EPA	Waters (RTP)	not yet awarded	--	1A-	Bioscreening	Suppo
32	Development of Test Systems to Assess Potential Toxicity and Neoplastic Transformation-Improved Screening of Chemical Transformation of C3H/10T½ Cells	EPA	Waters (RTP)	Heidelberger, University of Southern California	-/77 - --	1A1, 2B1, 1A4	Bioscreening, methods development	Toxic plast forma

*Funded by EPA pass-through in FY 75; transferred to ERDA base program in FY 76

	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
	1A1	Bioscreening	Carcinogenesis	Intravenuous, tissue culture media	Balb/C and C57B1/6J mice	Benzo(a)pyrene	Air	GA
	1A1, 1A4	Bioscreening	Cocarcinogenesis	Tissue culture media application	Cells (human, rodent)	Multiple pollutants, x-rays, fluorouracil	Multi	Coal, oil shale
	1A4, 2B1	Bioscreening, cellular toxicology	Cytotoxicity	Multi	Lung cells	Multiple pollutants	Air	Coal, oil shale
	1A4, 1A1, 1A2	Animal toxicology	Cytotoxicity	Multi	Cells (Chinese hamster)	Multiple pollutants, incl. Cd	Multi	GA
77	1A1	Animal toxicology	Carcinogenesis	Tissue culture media application	Hamster cells, mouse cells	Multiple pollutants, incl. pesticides, nitroso cpds	Multi	GA
	1A2	Bioscreening	Mutagenesis	Bacterial media application	Salmonella bacteria	Multiple pollutants, incl. PAH	Multi	Coal, oil shale
	1A2, 4C2	Bioscreening	Mutagenesis	Multi	Germ cells | mouse Somatic cells	Benzo(c)pyrene, dimethyl benzanthracene	Multi	Coal, oil
	1A1, 1A4, 2B1, 5A1	Cellular toxicology	Cocarcinogenesis	Tissue culture media application	Endometrial cells, rabbit	Hormones, PAH, dimethylbenzanthracene (DMBA)	Multi	GA
	1A4, 4B2, 1A2	Cellular toxicology	Biochemical changes	Tissue culture media application	Germ cells, mouse	Hormones, PAH, metals, DMBA, PaP	Multi	Coal
76	2B1	Animal toxicology	Toxicity	Injection	Spermatogonia	Cadmium	Multi	Fossil fuel
78	2B1, 2B2, 2B3	Cellular toxicology, animal toxicology	Toxicity	Inhalation	Lung tissue, enzymes	Pd, Pt, Hg	Air	Fossil fuel/ automotive
/79	2B1, 1A4, 5B1	Bioscreening	Cytotoxicity	In growth media	Lymphocyte	Multiple pollutants	Multi	Fossil fuel
79	2B2	Human health studies	Toxicity	Inhalation	Lung metabolism	NO_2, SO_2	Air	Fossil fuel
	2B2, 2B3	Human health studies	Toxicity, epidemiology	N/A	Physiological, biochemical measurement	N/A	Air	GA
80	2B2, 1A1, 3B3	Bioscreening, methods development	Carcinogenesis	In growth media	Microbial testors	Presumptive carcinogen metabolites	Multi	GA
	2B3	Bioscreening	Behavior modification	Inhalation	Behavior, CNS	Coal conversion pollutants	Air	Coal (g, l)
	1A-	Bioscreening	Support		N/A	N/A	Multi	GA
	1A1, 2B1, 1A4	Bioscreening, methods development	Toxicity, neoplastic transformation	Inhalation	Mouse fibroblasts	Particles	Air	GA

TABLE A-1 (CONTINUED)

	PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	H END
33	In vitro Screening of Selected Air Pollutants for Potential Carcinogenicity	EPA	Waters (RTP)	Schrechtman, Microbiological Associates	11/75 - 11/77	2B1, 2B2, 1A1, 1A2	Bioscreening	Carcin
34	Electroencephalographic and Behavioral Studies of Rats During Long Term Continuous Exposure to SO_2 and Particulate Matter	EPA	Lewkowski (Cincinnati)	Cooper, University of Cincinnati	5/75 - --	2B3, 4B2	Animal toxicology	Behavi
35	Development of Cytochemical Markers for Cell Transformation and Carcinogenesis	ERDA	Duda (ERDA)	Mayall, Lawrence Livermore Laboratory	3/77 - 7/77	2A2, 1A1, 2B1	Bioscreening	Carcin cytoto
36	Effects of Products of Coal and Oil Shale Conversion on Cell Cycle Kinetics and Chromatin Structure*	ERDA	Duda (ERDA)	Tobey, Los Alamos Scientific Laboratory	--	2B1, 1A4, 5A1, 5A2	Bioscreening cellular toxicology	Cytoto
37	Development of Differentiated Cell Culture Systems for Evaluation of Toxic Effects of Heavy Metals and Hydrocarbons	ERDA	Duda (ERDA)	Gerschenson, UCLA Laboratory of Nuclear Medicine and Radiation Biology	1/76 - 1/77	2B1, 1A4, 2B2	Cellular toxicology	Cytoto
38	Development of Permanent Epithelial Cell Lines with High Transformation Efficiency and Normal Function in Modification of Potential Carcinogens	ERDA	Duda (ERDA)	Kenney, Oak Ridge National Laboratory	--	2B1, 1A1, 1A4	Bioscreening	Carcin cytoto
39	Development of Method for Utilizing Teeth an an Indicator of Tissue Dose for Trace and Heavy Metals	ERDA	Duda (ERDA)	Stang, Brookhaven National Laboratory	1/76 - 1/78	2A1, 2A3, 1A4, 3A1	Bioscreening	Toxicit
40	Development of Non-Mammalian (Fish) Model for Quantitative Evaluation of Carcinogenicity of Coal Conversion Products	ERDA	Duda (ERDA)	Setlow, Brookhaven National Laboratory	1/76 - 1/77	2A2, 2A3, 1A1	Bioscreening	Carcin
41	Develop Tracheal Craft Model System for Evaluating Toxicity and Carcinogenicity of Polycyclic Hydrocarbons*	ERDA	Duda (ERDA)	Pal, Oak Ridge National Laboratory	--	2B3, 1A1, 1A4	Bioscreening	Carcin toxicit
42	Computer In vivo Detection of Mutations in Somatic and Germinal Cells	NIEHS	Malling (NIEHS)	Malling, NIEHS	--	2B1, 2B2, 4A1, 4A2, 1A2	Bioscreening, cellular toxicology	Mutagen
43	Development of a System for Detecting Lethal Mutations in Mice	NIEHS	Malling (NIEHS)	Roderick, The Jackson Laboratory	--	2B1, 1A2, 5A2	Bioscreening, cellular toxicology	Mutagen
44	Development of a New Mouse Strain to Maximize Sensitivity of a Point Mutation Assay	NIEHS	Malling (NIEHS)	Roderick, The Jackson Laboratory	--	2B1, 1A2, 5A2	Bioscreening	Mutagen
45	Amplification of Point Mutation System: Characterization of Mouse Esterases by Isoelectric Focusing	NIEHS	Malling (NIEHS)	Allen, Medical University of South Carolina	--	2B2, 1A2, 5A2	Bioscreening	Mutagen
46	Development of a Polygenic Assay for Induced Point Mutations in Mice	NIEHS	Malling (NIEHS)	Crenshaw, Georgia Institute of Technology	--	2B1, 1A2, 3A1, 5A2	Bioscreening	Mutagen
47	Detection of Point Mutations in Somatic Cells	NIEHS	Malling (NIEHS)	Nute, University of Washington	--	2B[illegible] 5A2	Bioscreening	Mutagen
48	Development of Faster, More Efficient and Less Costly Methods for Determining Teratogenic Changes	NIEHS	Malling (NIEHS)	Johnson, Research Triangle Institute	--	2B1, 2B2, [illegible] 1A3, 4C3	[illegible]ellular toxicology	Teratog
49	Mutagenesis in Cultured Lymphocytes	NIEHS	Malling (NIEHS)	Bloom, Columbia University	--	2B[illegible], 2B3, 1A2, 5A2	[illegible]	[illegible]
50	Multiple Loci Screen for Mutations in Mammalian Cells	NIEHS	Malling (NIEHS)	Siciliano, University of Texas Cancer Center	--	2B2, 1A2	Cellular toxicology, bioscreening	Mutagen
51	Development of DNA Repair for Monitoring Human Health	NIEHS	Malling (NIEHS)	Mitchell, Stanford Research Institute	--	2B2, 1A1, 1A2, 1A4	Cellular toxicology, bioscreening	Biochem changes

E	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
/77	2B1, 2B2, 1A1, 1A2	Bioscreening	Carcinogenicity	In growth media	Fibroblasts, microbial	Environmental pollutants, solvents	Air	GA
	2B3, 4B2	Animal toxicology	Behavior/EEGs	Inhalation	CNS (rat)	SO_2 particles, auto exhaust	Air	Fossil fuel/ general
7	2A2, 1A1, 2B1	Bioscreening	Carcinogenesis, cytotoxicity	Tissue culture media application	Syrian hamster and Syrian hamster embryo	Multiple pollutants	Multi	Coal, oil shale, geothermal
	2B1, 1A4, 5A1, 5A2	Bioscreening cellular toxicology	Cytotoxicity	Tissue culture	Cell cultures	Multiple pollutants	Multi	Coal, oil shale
7	2B1, 1A4, 2B2	Cellular toxicology	Cytotoxicity	Tissue culture	Various cell cultures	DMBA, BaP, benzo(σ)anthracene, methyl cholanthrene, Pb and Na nitrate	Multi	GA
	2B1, 1A1, 1A4	Bioscreening	Carcinogenesis, cytotoxicity	Tissue culture media application	Epithelial cell tissues	Carcinogens, polycyclic hydrocarbons	Multi	GA
8	2A1, 2A3, 1A4, 3A1	Bioscreening	Toxicity	Multi	Teeth (human)	Trace and heavy metals	Multi	GA
7	2A2, 2A3, 1A1	Bioscreening	Carcinogenicity	Multi	Poecilia formosa (fish)	Coal conversion products	Water	Coal, oil shale
	2B3, 1A1, 1A4	Bioscreening	Carcinogenicity, toxicity	Implantation	Trachea	Polycylic and aromatic hydrocarbons	Air	GA
	2B1, 2B2, 4A1, 4A2, 1A2	Bioscreening, cellular toxicology	Mutagenesis	In vivo	Mouse sperm	Mutagens	Multi	GA
	2B1, 1A2, 5A2	Bioscreening, cellular toxicology	Mutagenesis	In vivo	Mouse	Radiation, chemicals	Multi	GA
	2B1, 1A2, 5A2	Bioscreening	Mutagenesis	N/A	Mice	N/A	Multi	GA
	2B2, 1A2, 5A2	Bioscreening	Mutagenesis	N/A	Mice	N/A	Multi	GA
	2B1, 1A2, 3A1, 5A2	Bioscreening	Mutagenesis	N/A	Mice	Multiple pollutants, incl. mitomycin-C, TEM, MMS	Multi	GA
	2B[illegible] 5A2	Bioscreening	Mutagenesis	N/A	Human red blood cells	N/A	Multi	GA
	2B1, 2B2, [illegible] 1A3, 4C3	[illegible]ellular toxicology	Teratogenesis	Multi	Rat, hamster, mouse, embryos	Dipterex, asbestos and drinking water, SO_x, NO_x, S and N compounds	Water	Coal
	2B2, 2B3, 1A2, 5A2	[illegible]	[illegible]genesis	Bacterial media	Human lymphocytes, Salmonella, mouse myeloma	2-Florenamine	Multi	GA
	2B2, 1A2	Cellular toxicology, bioscreening	Mutagenesis	Tissue culture media application	Chinese hamster ovary cells, mammalian somatic cells	Multiple pollutants	Multi	GA
	2B2, 1A1, 1A2, 1A4	Cellular toxicology, bioscreening	Biochemical changes	In vitro	Various targets, DNA	Multiple pollutants	Multi	GA

TABLE A-1 (CONTINUED)

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PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	E END
A Modified Host-Mediated Assay Using Human Cells	NIEHS	Malling (NIEHS)	Huang, New York State Dept. of Health, Roswell Park Div.	--	2B1, 1A1, 1A2	Cellular toxicology, bioscreening	Cytote
Developmental Toxicology Indicators	NIEHS	Malling (NIEHS)	Dixon, NIEHS	--	2B3	Human health	Terate
Effects of Environmental Pollutants in Relation to Age: Toxicity of Compounds from Coal Gasification	EPA	Stara (Cincinnati)	Kostial, Institute for Medical Research and Occupational Health; Zagreb, Yugoslavia	3/76 - --	3A1, 3B1	Animal toxicology, human health studies	Toxicl
Scanning Electron Microscopic Examination of the Effects of Air Pollutants on Pulmonary Systems	EPA	Gardner/ Waters (RTP)	Aranyi, Illinois Institute of Technology Research Institute	4/76 - 9/76	3A1	Cellular toxicology	Toxicl
Studies on the Relationship Between Carcinogen Metabolism in the Alveolar Macrophage and the Induction of Lung Cancer	EPA	Waters (RTP)	Northrop Services	12/76 - /80 (est)	3B3	Bioscreening, animal toxicology	Carcir
Investigation of Effects of Prolonged Inhalation of As, Ni, and Cr- Enriched Fly Ash in Syrian Golden Hamsters	EPA	Moore (Cincinnati)	Wehner, Battelle, Pacific Northwest Laboratories	9/76 - 9/79	3B1, 4B2	Animal toxicology	Toxicl
Comparative Toxicological Assessment of Fly Ash from Western and Eastern Coal	EPA	Pepelko (Cincinnati)	Huntington Research Corporation	-/76 - --	3B3, 4B2, 4B3, 4D1, 1A4	Animal toxicology	Toxicl
Deposition, Retention and Dosimetry of Inhaled Reaction Products Which May Result from SO_2-Particle Reactions	ERDA	Schulman (ERDA)	Snipes, Lovelace Foundation	1/76 - 7/78	3B1, 3A1	Animal toxicology	Cytote
Metabolism of Inhaled Trace Metal Effluents from Combustion Processes	ERDA	Schulman (ERDA)	Cuddihy, Lovelace Foundation	1/76 - 1/78	3A1, 3B1, 4B2	Animal toxicology	Cytote
Influence of Diet on the Gastro-Intestinal Absorption of Cadmium	ERDA	Schulman (ERDA)	Walburg, University of Tennessee	--	3A1	Animal toxicology	--
Synthesis of Labeled Organic and Organometallic Compounds for Use in Metabolism and Catabolism Studies*	ERDA	Schulman (ERDA)	Wolf, Brookhaven National Laboratory	7/76 - 12/78	3A1, 3B3	Animal toxicology	Biochc change
Metabolism and Disposition of Selected Radiolabelled Hydrocarbons and Some of Their Chemically Reactive Epoxides by the Isolated, Perfused Rabbit Lung and by Solubilized, Reconstituted Pulmonary Biotransformation Systems	NIEHS	Dixon (NIEHS)	Bend, NIEHS	8/75 - --	3A1, 4B3	Animal toxicology	Biochc change
Environmental Teratology Information Center (ETIC)	NIEHS	Dixon (NIEHS)	Staples, Oak Ridge National Laboratory	8/75 - --	3B1, 3B2, 3B3, 5A1, 5A2	Human health	Terate
Regulation of Neural Distribution of Lead	NIEHS	Dixon (NIEHS)	O'Tauma, University of North Carolina	9/75 - 8/78	3A1, 3B1, 5A1	Animal toxicology	Biochc change
Function of Metallothionein in Heavy Metal Metabolism	NIEHS	Dixon (NIEHS)	Brady, University of South Dakota	9/75 - 8/78	3A1, 3B1, 5A1	Animal toxicology	Biochc change
Mechanisms of Heavy Metal Toxicity	NIEHS	Dixon (NIEHS)	Woods, NIEHS	8/76 - --	3A1	Animal toxicology	Toxicl
Effects of Microwave Radiation on the Nervous System	NIEHS	Dixon (NIEHS)	Lovely, University of Washington	8/76 - --	4B2 3B2	Animal toxicology	Toxicl
Biological Effects of 60 Hertz Electric Fields	NIEHS	Dixon (NIEHS)	Marino, Research Foundation of SUNY; SUNY Upstate Medical Center	2/77 - 1/80	3A1	Animal toxicology	Biochc change
Respiratory Tract Deposition Models	NIEHS	Dixon (NIEHS)	Raabe, Lovelace Foundation	8/75 - --	3A1, 5A1, 4D1	Risk/extrapolation	Toxicl

NVESTI-IATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABI TECHNOLO
York of vell	--	2B1, 1A1, 1A2	Cellular toxicology, bioscreening	Cytotoxicity	Tissue culture media application	Human lymphoid cells	Cyclophosphamide, Folpet and other pesticides	Multi	GA
5	--	2B3	Human health	Teratogenesis	N/A	Human	Environmental pollutants	Multi	GA
stitute Research ional reb,	3/76 - --	3A1, 3B1	Animal toxicology, human health studies	Toxicity	Ingestion, inhalation	Rats, humans	Cd, Hg, Pb, Mn	Multi	GA
inois f Research	4/76 - 9/76	3A1	Cellular toxicology	Toxicity	--	Alveolar macrophage	Pb, Mn, Ni, Cd oxides	Air	Fossil fuel
rvices	12/76 - /80 (est)	3B3	Bioscreening, animal toxicology	Carcinogenesis	In growth media, intubation, inhalation	Alveolar macrophage, hamsters, rats	BaP, anthracene	Multi	Fossil fuel
elle, thwest	9/76 - 9/79	3B1, 4B2	Animal toxicology	Toxicity	Inhalation	Pulmonary	Fly ash (Ni enriched)	Air	Coal
Research	-/76 - --	3B3, 4B2, 4B3, 4D1, 1A4	Animal toxicology	Toxicity	Inhalation	Pathology, blood chemistry	Fly ash (western, eastern coals)	Air	Coal
lace	1/76 - 7/78	3B1, 3A1	Animal toxicology	Cytotoxicity	Aerosol	Syrian hamsters, lung	Ammonium sulfate, sulfuric acid, SO_2	Air	Fossil fuel
elace	1/76 - 1/78	3A1, 3B1, 4B2	Animal toxicology	Cytotoxicity	Aerosol	Beagles, Syrian hamsters, rats, other cell systems	Trace metals Ag, Cd, V, Se, Ni, As	Air	GA
ver-essee	--	3A1	Animal toxicology	--	Per os	Gastro-intestinal tract	Cadmium	Diet	Fossil fuel, solar
aven oratory	7/76 - 12/78	3A1, 3B3	Animal toxicology	Biochemical changes	N/A	N/A	Organics, organometallics	N/A	GA
	8/75 - --	3A1, 4B3	Animal toxicology	Biochemical changes	Perfusion	Rabbit lung, rat liver	Styrin oxide, unsat. hydrocarbons	Multi	GA
Ridge oratory	8/75 - --	3B1, 3B2, 3B3, 5A1, 5A2	Human health	Teratogenesis	N/A	N/A	Multiple pollutants	Multi	GA
ver-h	9/75 - 8/78	3A1, 3B1, 5A1	Animal toxicology	Biochemical changes	Multi	Neural tissues	Pb, Ca	Multi	GA
rsity ota	9/75 - 8/78	3A1, 3B1, 5A1	Animal toxicology	Biochemical changes	Multi	Rat lungs, liver, kidneys; rats	Cd, Zn, Cu, Hg, Ni, Tl, metallothionein	Multi	GA
	8/76 - --	3A1	Animal toxicology	Toxicity	Inhalation	Several animal species	Trace metals	Multi	GA
er-ing-	8/76 - --	4B2 3B2	Animal toxicology	Toxicity	In vivo	Rat physiology, CNS	Microwave radiation	Multi	GA
arch f pstate er	2/77 - 1/80	3A1	Animal toxicology	Biochemical changes	Immersion	Mice, rats, rabbits (physiology, reprod, behavior)	60 hertz electric fields	Multi	GA
ace	8/75 - --	3A1, 5A1, 4D1	Risk/extrapolation	Toxicity	Aerosol	N/A	Multiple pollutants	Multi	GA

TABLE A-1 (CONTINUED)

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PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEAL END P
Respiratory Tract Deposition of Inhaled Aerosols	NIEHS	Dixon (NIEHS)	Yu, State University of New York, Buffalo	12/75 - 11/78	3A1, 1A4, 4A2, 5A1, 4D1	Animal toxicology	Toxicity
Factor Affecting Irritant Potency of Gases and Aerosols	NIEHS	Dixon (NIEHS)	Amdur, Harvard School of Public Health	11/75 - 10/78	3B1, 3B2, 3B3, 5A1	Risk/extrapolation	Toxicity
Compartmental Models for Body Burden of Pollutants	NIEHS	Dixon (NIEHS)	Marcus, University of Maryland	12/75 - 11/77	3B1, 3B2, 3B3	Risk/extrapolation	Toxicity
Trace Element Deposition in Ambient Aerosol Inhalation	NIEHS	Dixon (NIEHS)	Winchester, Florida State University	1/76 - 6/79	3A1, 3B3	Human health	Toxicity
Regional Deposition of Inhaled Particles in Man	NIEHS	Dixon (NIEHS)	Lippman, New York University Medical Center	7/76 - 6/79	3A1, 3B3, 5A1	Human health	Toxicity
Development of NMR Spectroscopic Methods for Characterizing Specific Binding (Electronic and Covalent Bonding) Modes of Organics and Inorganics Associated with Non-Nuclear Energy Technologies	NIEHS	Dixon (NIEHS)	McKinney, NIEHS	8/76 - --	5A2	Risk extrapolation	Toxicity
Relationship of Metabolism, Fate, and Toxicology of Particulates and Organic Compounds	NIOSH	Baier (NIOSH)	Bruckner, NIOSH-Rockville	5/75 - 5/80	3B3	Cellular toxicology	Biochemi changes
Effects of H_2SO_4 Aerosols on Human Respiratory Function	EPA	Haak (RTP)	Horvath, University of California	-/77 - --	4A2	Human health studies	Toxicity
Effects of Nitrogen Dioxide on Pulmonary Function in Human Subjects with Asthma and Chronic Bronchitis	EPA	Ketcham (RTP)	Kerr, University of Maryland	6/74 - 11/76	4A2, 4A1	Human health studies	Pulmonar function
Effect of Respirable Sulfates and H_2SO_4 Mists Upon Respiratory Function in Normal Human Subjects	EPA	Haak (RTP)	Kerr, University of Maryland	1/77 - -	4A2	Human health studies	Pulmonar function
Determination of the Effects of Material from Alternate Energy Sources on Upper Respiratory Tract Clearance Mechanisms	EPA	Gardner (RTP)	Adalis, Ball State University	10/75 - 5/79	4B2, 4B3	Cellular toxicology	Mucocili function
Air, Water and Multi-Route Exposure and Health Effects from Pollutants Associated with Energy Development	EPA	Stara (Cincinnati)	In-house support	10/76 - 10/77	4A1, 4A2, 4B2	Human health studies	Human he
Establishment of a Chemical Repository for Alternate Energy Source Material for Toxicity Testing	EPA	Coffin (RTP)	Guerin/Wood, Oak Ridge National Laboratory	-- - 9/78	4C1, 4C2, 1A1, 1A2, 1A3, 1A4, 2B1	Bioscreening, cellular/animal toxicology	Support/ toxicity
Evaluation of Potential Health Hazards Associated with Exposure to Indoor Air Pollutants	EPA	French (RTP)	Allen/Swift, Geomet, Inc.	3/76 - 8/77	4A2, 1A4	Human health studies	Toxicity
Model for Measuring the Health Impact from Changing Levels of Ambient Air Pollution	EPA	Riggan (RTP)	Carnow, University of Illinois	10/76 - 1/78	4D1, 4A1	Human health studies/model development	Toxicity
Effects of Pollutants from Coal Burning and Coal Gasification on the Immune System	EPA	Graham (RTP)	Zarkower, Penn State University	10/76 - 9/79	4B2, 4D1, 5B1, 1A1	Bioscreening, animal toxicology	Immune dysfunct
To Determine Effects of Pollutants from Alternate Energy Sources on Pulmonary Antiviral Mechanisms	EPA	Graham (RTP)	Schiff/Ehrlich Illinois Institute of Technology Research Institute	12/76 - --	4D1, 5A1	Cellular toxicology	Toxicity
Effect of Material from Alternate Energy Sources on Whole Animal Defense Systems	EPA	Graham (RTP)	Rowlands, Southwest Foundation for Research and Education	-/76 - 10/79	4D1, 5A1, 5A2	Animal toxicology	Whole a immune
Effect of Coal Gasification Products on the Pulmonary Function Defense System Against Infectious Disease (Bacterial)	EPA	Graham (RTP)	to be awarded	-/77 - --	4B1, 4D1	Animal toxicology	Toxicity
Evaluate Effects of Chronic or Intermittent Exposures to Respirable Particles and Mists Using Mouse Pulmonary Infectivity Model	EPA	Gardner (RTP)	Ehrlich, Illinois Institute of Technology Research Institute	8/75 - 6/77	4B1, 4B2	Animal toxicology	Toxicity

STI-ION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
er-rk,	12/75 - 11/78	3A1, 1A4, 4A2, 5A1, 4D1	Animal toxicology	Toxicity	Aerosol	Model of human respiratory tract	Particles	Multi	GA
ic	11/75 - 10/78	3B1, 3B2, 3B3, 5A1	Risk/extra-polation	Toxicity	Aerosol	Guinea pig respiration	O_3, SO_2	Multi	GA
nd	12/75 - 11/77	3B1, 3B2, 3B3	Risk/extra-polation	Toxicity	Multi	N/A	CO; bone-seeking metals	Multi	GA
	1/76 - 6/79	3A1, 3B3	Human health	Toxicity	Aerosol	Human respiratory tract	Mixed particles	Multi	GA
ork ical	7/76 - 6/79	3A1, 3B3, 5A1	Human health	Toxicity	Aerosol	Donkey lungs, human respiration	Fe_2O_3 microspheres	Multi	GA
S	8/76 - --	5A2	Risk extrapola-tion	Toxicity	Aerosol	Body fluids and tissues	Multiple pollutants	Multi	GA
H-	5/75 - 5/80	3B3	Cellular toxi-cology	Biochemical changes	--	--	Multiple pollutants	Multi	GA
r-rnia	-/77 - --	4A2	Human health studies	Toxicity	Inhalation	Cardiopulmonary	H_2SO_4 mists	Air	Fossil fuel
ty	6/74 - 11/76	4A2, 4A1	Human health studies	Pulmonary function	Inhalation	Pulmonary	NO_2, air pollutants	Air	Fossil fuel
ty	1/77 - -	4A2	Human health studies	Pulmonary function	Inhalation	Pulmonary	$SO_4^=$, H_2SO_4 mists	Air	Fossil fuel
tate	10/75 - 5/79	4B2, 4B3	Cellular toxi-cology	Mucocilliary function	In growth media	Trachea cilliary escalator	Particles, trace metals (Mn oxides)	Air	Fossil fuel
rt	10/76 - 10/77	4A1, 4A2, 4B2	Human health studies	Human health	Inhalation	Health	Multiple pollutants	Multi	GA
ak	-- - 9/78	4C1, 4C2, 1A1, 1A2, 1A3, 1A4, 2B1	Bioscreening, cellular/animal toxicology	Support/ toxicity	N/A	N/A	Environmental pollutants	Multi	GA
	3/76 - 8/77	4A2, 1A4	Human health studies	Toxicity	Inhalation	Humans	Indoor air pollutants	Air	Conserva-tion
-is	10/76 - 1/78	4D1, 4A1	Human health studies/model development	Toxicity	Inhalation	Humans	Air pollutants	Air	Convervation
ity	10/76 - 9/79	4B2, 4D1, 5B1, 1A1	Bioscreening, animal toxi-cology	Immune system dysfunction	Inhalation, in cell culture media	Respiratory immune system	Environmental pollutant, arsine	Air	Coal (g, l)
itute	12/76 - --	4D1, 5A1	Cellular toxicology	Toxicity	In growth media	Respiratory epithelium	Environmental pollutants	Air	Fossil fuel
itute									
hwest Educa-	-/76 - 10/79	4D1, 5A1, 5A2	Animal toxi-cology	Whole animal immune systems	Inhalation	Respiratory tissues	Environmental pollutants	Air	Fossil fuel
	-/77 - --	4B1, 4D1	Animal toxicology	Toxicity	Inhalation	Pulmonary anti-bacterial defense system	Environmental pollutants	Air	Coal (g)
ois earch	8/75 - 6/77	4B1, 4B2	Animal toxicology	Toxicity	Inhalation	Pulmonary infectivity	Particles, H_2SO_4 mists	Air	Fossil fuel

TABLE A-1 (CONTINUED)

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	PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	E
1	Assessment of the Postnatal Development and Function of the CNS of Monkeys Exposed to Tritiated Water (HTO) from Conception to Birth or Weaning	EPA	Cahill (RTP)	Dawson Research Corporation	1/76 - 12/77	4B2, 4D1, 4B1, 3B2	Animal toxicology	Toxi
2	Investigation of the Neoplastic and Life-span Effects on Potentially Sensitive Populations of Rats Chronically Exposed to Tritiated Water (HTO)	EPA	Wright (RTP)	Jones, Stanford Research Institute	11/75 - 2/77	4B1, 3B2, 4B2, 4D1	Animal toxicology	Toxi plas
3	Effects of Pollutants from Energy Consumption and Environmental Trace Metals on Lung Metabolism	EPA	Lee (Cincinnati)	Mustafa, UCLA	6/75 - -/78	4B1, 4B3, 4B2, 5C1	Animal toxicology	Toxi funct
4	Study of Metabolic and Physiologic Measurements in Populations with Long-Term Exposure to Pollution from Coal Combustion	EPA	French (RTP)	Mostardi, University of Akron	10/76 - --	4A1	Human health studies	Toxi bidi tali
5	Determination of Carcinogenic, Mutagenic, and Teratogenic Potential of Five Compounds (methyl benzimidazole, dibenzofuran, methyl benzofuran, 1,2,4-trimethyl benzene, thallium) Generated from Coal Conversion and Utilization to Which Man is Exposed Orally and by Inhalation	EPA	Stara (RTP)	Hart, Litton Bionetics	--	4C2, 1A3, 1A2, 4C3, 4B2	Bioscreening animal toxicology	Toxi geni geni toge
6	Epidemiology Study of the Health Effects of Energy Production By-Products in Drinking Water	EPA	Craun (Cincinnati)	--	-/77 - --	4A1	Human health studies	Toxi
7	Evaluate the Influence of Inhalation of Acid Aerosols, H_2SO_4, $SO_3^=$, HNO_3 and Particles on Production of Chronic Lung Disease in Rats, Guinea Pigs, and Primates	EPA	Gardner/Fairchild (RTP)	Tyler, University of California, Davis	1/76 - 6/77	4B2, 4B3, 4D1	Animal toxicology	Toxi
8	Compare Effects of Respirable Particles, Gases, and Mists Using Small Airway Resistance in Donkeys as the Model for Pulmonary Irritation	EPA	Gardner (RTP)	Lippman, New York University	6/76 - 6/78	4D1, 4B2	Animal toxicology	Toxi
9	CLEANS/CLEVER Operation and Maintenance	EPA	Crider/Strung (RTP)	to be awarded	8/76 - --	4B2	Human health studies	Supp
10	Aerosol Addition to CLEANS	EPA	Crider (RTP)	Environmental Research and Technology	6/75 - 7/77	4B2	Human health studies - support	Supp
11	Stationary and Mobile Facilities for Study of Health Effects of Environmental Contaminants (CLEANS/CLEVER)	EPA	Crider (RTP)	Marsh, Computer Science Corp.	5/73 - 8/76	4B2	Human health studies - support	Supp
12	Operation and Maintenance of Community Health Air Monitoring Program (CHAMP) to Quantitate Air Pollution Exposure in Selected Health Study Areas	EPA	Hinton (RTP)	(Raphael), Rockwell International Corp.	1/75 - 12/76?	4A1	Human health studies - support	Supp
13	The Effect of Whole Animal Exposure to Acid Mists on Pulmonary Metabolism of BAP in the Isolated Perfused Lung Model	EPA	Kommineni (RTP)	Bingham, University of Cincinnati	7/75 - --	4C2, 5A1, 5A2, 1A1, 1A2	Animal/cellular toxicology	Carci
14	An Environmental Health Study of Lead in Teeth	EPA	Stara (Cincinnati)	Wilkinson, Delaware State College	6/74 - 6/76	4B3, 2A3, 2B3	Human health studies	Physi (leve in te
15	Cytogenetic Studies of Lung Cells Following Inhalation of Fly Ash, Chemical Mutagens and Effluents from Power Related Industry	ERDA	Roderick (ERDA)	Brooks, Lovelace Foundation	1/76 - 1/78	4C2, 1A2, 5A1, 5A2	Cellular toxicity	Cyto mutag
16	Factors Influencing Cross-Placental Transfer and Teratogenicity of Metallic Pollutants	ERDA	Roderick (ERDA)	Sikov, Battelle, Pacific Northwest Laboratories	1/76 - 7/78	4C3, 3A1, 3B1	Animal toxicology	Terat
17	Genetic Effects from Electric Fields at the Chromosomal Level of Drosophila	ERDA	Roderick (ERDA)	Hungate, Battelle, Pacific Northwest Laboratories	--	4C2, 1A2	Animal toxicology	Bioch chang
18	Use of the Mouse Specific-Locus Method to Quantify the Gene Mutation Hazard from Mutagens Associated with Non-Nuclear Energy Technologies	ERDA	Roderick (ERDA)	Russell, Oak Ridge National Laboratory	--	4C2, 1A2	Cellular toxicology	Mutag
19	Mutagenicity and Carcinogenicity of Energy-Related Pollutants in Cultured Mammalian Cell Systems	ERDA	Roderick (ERDA)	Hsie, Oak Ridge National Laboratory	--	4C1, 4C2, 1A1, 1A2	Cellular toxicology	Mutag carci

INVESTI-ILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
search on	1/76 - 12/77	4B2, 4D1, 4B1, 3B2	Animal toxicology	Toxicity/behavior	Ingestion	Whole animal (monkeys), embryos	Tritiated water (HTO)	Water	Nuclear
anford	11/75 - 2/77	4B1, 3B2, 4B2, 4D1	Animal toxicology	Toxicity, neoplasticity	Ingestion	Pregnant female rats	Tritiated water (HTO)	Water	Nuclear
UCLA	6/75 - -/78	4B1, 4B3, 4B2, 5C1	Animal toxicology	Toxicity/lung function	Inhalation	Lung metabolism	NO_2, ozone, SO_x, SO_4's, trace metals, H_2SO_4	Air	Fossil fuel
Univer-xron	10/76 - --	4A1	Human health studies	Toxicity (morbidity, mortality)	Inhalation	Lung function	Environmental pollutants	Air	Coal
ton	--	4C2, 1A3, 1A2, 4C3, 4B2	Bioscreening animal toxicology	Toxicity, carcinogenicity, mutagenicity, teratogenicity	Inhalation, intubation (in vivo), in growth media (in vitro)	S. typhimurium, rats	Environmental pollutants, methyl benzimidazole, dibenzofuran, methyl benzofuran, 1,2,4 trimethyl benzene, thallium	Air, water	Coal (g, l)
	-/77 - --	4A1	Human health studies	Toxicity	Ingestion	Humans	Environmental water pollutants	Water	GA
iver-alifor-a	1/76 - 6/77	4B2, 4B3, 4D1	Animal toxicology	Toxicity	Inhalation	Pulmonary	H_2SO_4, SO_3^-, HNO_3, particles	Air	Fossil fuel
New York y	6/76 - 6/78	4D1, 4B2	Animal toxicology	Toxicity	Inhalation	Donkey and human lung model	Particles, $(NH_4)_2$, SO_4, H_2SO_4	Air	Fossil fuel
rded	8/76 - --	4B2	Human health studies	Support	Inhalation	Pulmonary	Criteria pollutants	Air	Fossil fuel
ntal and y	6/75 - 7/77	4B2	Human health studies - support	Support	N/A	Analytical	Criteria pollutants	Air	Fossil fuel
mputer orp.	5/73 - 8/76	4B2	Human health studies - support	Support	Inhalation	Support	Criteria pollutants	Air	ssil l
, Rockwell onal	1/75 - 12/76	4A1	Human health studies - support	Support	N/A	Analytical	Criteria pollutants	Air	il
Univer-incinnati	7/75 - --	4C2, 5A1, 5A2, 1A1, 1A2	Animal/cellular toxicology	Carcinogenicity	Inhalation/growth media	Perfused lung tissue	BaP	Air	Fossil fu l
, Delaware lege	6/74 - 6/76	4B3, 2A3, 2B3	Human health studies	Physiological (levels of Pb in teeth)	Ingestion, inhalation	Teeth	Lead	Multi	Fossil fuel automotive
ovelace n	1/76 - 1/78	4C2, 1A2, 5A1, 5A2	Cellular toxicity	Cytotoxicity, mutagenesis	Aerosol	Syrian and Chinese hamster	Fly ash	Air	GA
ttelle, orth-ratories	1/76 - 7/78	4C3, 3A1, 3B1	Animal toxicology	Teratogenesis	Multi	Rat	Lead, vanadium	Multi	GA
Battelle, orth-ratories	--	4C2, 1A2	Animal toxicology	Biochemical changes	Immersion	Drosophila chromosomes, microorganisms	Electrical fields	Air	GA
Oak Ridge Laboratory	--	4C2, 1A2	Cellular toxicology	Mutagenesis	Varied	Mice	SO_2; Benzo(a) pyrene	Multi	GA
Ridge Laboratory	--	4C1, 4C2, 1A1, 1A2	Cellular toxicology	Mutagenesis, carcinogenesis	Tissue culture media application	Chinese hamster ovary, mouse cells	Benzo(a)pyrene and metabolites	Multi	GA

TABLE A-1 (CONTINUED)

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	PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HE... END ...
110	The Use of Selected Teratogenic Test Systems to Identify Hazardous Agents Associated with Non-Nuclear Energy Technologies, and to Determine Effective Levels of Such Agents*	ERDA	Roderick (ERDA)	Russell, Oak Ridge National Laboratory	1/76 - 7/77	4C3, 1A3	Animal toxicology	Teratog...
111	The Mouse Oocyte System as a Monitor of Chemical Toxicity	ERDA	Roderick (ERDA)	Dobson, Lawrence Livermore Laboratory	1/76 - 7/77	4B1, 4C3, 1A3	Bioscreening, cellular toxicology	Toxicity
112	Teratogenic and Mutagenic Effects of Trace Metals and Carcinogenic Hydrocarbons on Cultured Mammalian Cells	ERDA	Roderick (ERDA)	de Vellis, UCLA Laboratory of Nuclear Medicine and Radiation Biology	--	4C1, 4C2, 4C3, 1A1, 1A2, 1A3	Cellular toxicology	Teratog... mutagen... carcino...
113	Evaluate the Effect of Low Level Chronic Radiation on Mammalian Brain Development over Several Generations*	ERDA	Roderick (ERDA)	Zamenhof, UCLA Laboratory of Nuclear Medicine and Radiation Biology	--	4C3, 4C2	Animal toxicology	Toxicity teratog...
114	Combined Effects of Acute and Chronic Exposure to CO, NO_2, SO_2, and Fly Ash*	ERDA	Stuart/Smith (ERDA)	Craig, Battelle, Pacific Northwest Laboratories	1/76 - 6/78	4B2, 4B3, 4A1, 5A1	Animal toxicology	Toxicity
115	Effects of Sulfur Pollutants on Lung Physiology and Biochemistry*	ERDA	Stuart/Smith (ERDA)	Loscutoff, Battelle, Pacific Northwest Laboratories	--	4B2, 4B3, 5D1, 5A1, 5C1, 4D1	Animal toxicology	Toxicity biochem... changes
116	The Effect of Acid Sulfate Particles and SO_2 on the Anti-Bacterial, Anti-Viral and Particle Clearance Mechanisms in the Lung*	ERDA	Stuart/Smith (ERDA)	Hahn, Lovelace Foundation	--	4B2, 4B3, 3A1	Animal toxicology	Toxicity
117	Cardiopulmonary Injury and Repair after Inhaled Acid Sulfate Aerosols*	ERDA	Stuart (ERDA)	Mauderly, Lovelace Foundation	1/76 - 1/78	4B2, 5B1	Animal toxicology	Toxicity
118	Effects of Carbon Monoxide, Hydrogen Sulfide and Other Energy Products on Neutrons in Tissue Culture*	ERDA	Stuart (ERDA)	Tobias, Lawrence Berkeley Laboratory	7/76 - 10/76	4B2	Cellular toxicology	Biochem... changes
119	Interactions of Atmospheric Contaminants with Respiratory Structure and Receptors at both Biochemical and Functional Levels*	ERDA	Stuart (ERDA)	Morrow, University of Rochester Medical School	--	4B2, 3A1, 4B3, 5A1, 4A2	Cellular toxicology	Cytotox...
120	Temporal Aspects of Tumor Response to Individual and Mixed Carcinogen Exposure*	ERDA	--	Albert, New York University	--	4C1	Cellular toxicology	Carcino...
121	The Role of Irritant Gases on the Susceptibility of Respiratory Tract Epithelium to Tumor Induction*	ERDA	Stuart (ERDA)	Creasia, Oak Ridge National Laboratory	--	4C1, 2B1, 5A1, 1A1	Cellular toxicology	Carcino...
122	Organ Culture Studies with Tracheal Mucosa Pre-Exposed *in vivo* to Polycyclic Hydrocarbons*	ERDA	Stuart (ERDA)	Marchok, Oak Ridge National Laboratory	--	4C1, 1A1, 2B1	Cellular toxicology	Cytotox... carcino...
123	The Influence of Irritant Gases on Lung Tumor Induction in Mice Exposed to Urethane*	ERDA	Stuart (ERDA)	Jones, Lawrence Berkeley Laboratory	--	4C1, 1A1, 3A1, 5A1	Animal toxicology	Carcino...
124	Multi-mode Scanning Electron Microscopic Analysis of Individual Pollutant Particles in Lung*	ERDA	Stuart (ERDA)	Hayes, Lawrence Berkeley Laboratory	--	4B2, 3A1, 3B3	Cellular toxicology	Toxicit...
125	The Role of 1,2 Benzanthracene in Enhancing Hepatic Tumor Development in Rats fed AAF*	ERDA	Stuart (ERDA)	Peraino, Argonne National Laboratory	--	4C1, 1A1, 3B3, 5A1	Animal toxicology	Carcino...
	... of Energy-Related Pollutants on Male and ... Reproductive Tract Function	NIEHS	Dixon (NIEHS)	Lucier, NIEHS	8/75 - --	4B2, 4B3, 4C3	Animal toxicology	Teratog...
	... Microwave Fields on the Mammalian Central ...	NIEHS	Dixon (NIEHS)	McRee, NIEHS	8/75 - --	4B2, 4B3, 5A1	Animal toxicology	Toxicit...

INVESTI-LIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
ak Ridge aboratory	1/76 - 7/77	4C3, 1A3	Animal toxicology	Teratogenesis	Varied	Mice (embryos)	X-rays; benzo(a)pyrene	Multi	GA
rence Laboratory	1/76 - 7/77	4B1, 4C3, 1A3	Bioscreening, cellular toxicology	Toxicity	Tissue culture media application	Mice	Chloroform, ethyl methane sulfonate, sodium sulfite, platinum chloride	Multi	GA
UCLA of dicine ion	--	4C1, 4C2, 4C3, 1A1, 1A2, 1A3	Cellular toxicology	Teratogenesis, mutagenesis, carcinogenesis	Tissue culture media application	Mammalian cells	Pb, Cd, dimethyl benzanthracene (DMBA)	Multi	GA
UCLA of dicine ion	--	4C3, 4C2	Animal toxicology	Toxicity, teratogenesis	Immersion	Mammalian brain (rat)	Radiation	Air	Nuclear
elle, th-tories	1/76 - 6/78	4B2, 4B3, 4A1, 5A1	Animal toxicology	Toxicity	Aerosol	Pulmonary	NO_2, SO_2, CO, fly ash	Air	Fossil fuel
Pacific	--	4B2, 4B3, 5D1, 5A1, 5C1, 4D1	Animal toxicology	Toxicity, biochemical changes	Aerosol	Lung (guinea pigs)	Sulfur pollutants	Air	GA
lace	--	4B2, 4B3, 3A1	Animal toxicology	Toxicity	Aerosol	Pulmonary system of Syrian hamsters, mice	H_2SO_4, acid sulfates	Air	GA
Lovelace	1/76 - 1/78	4B2, 5B1	Animal toxicology	Toxicity	Aerosol	Cardiopulmonary system of guinea pigs, dogs	H_2SO_4, acid sulfates	Air	GA
rence	7/76 - 10/76	4B2	Cellular toxicology	Biochemical changes	In media	Nerve cells	CO, H_2S	Multi	GA
iver-hester ool	--	4B2, 3A1, 4B3, 5A1, 4A2	Cellular toxicology	Cytotoxicity	Tissue culture media application, in vivo	Neuroblastoma and mammalian cells, pulmonary system	CO, particulates, NO_x	Air	GA
York	--	4C1	Cellular toxicology	Carcinogenesis	In vivo	Mouse, rat, and hamster lung	Ionizing radiation, UV light, benzo(a) pyrene, 4-nitro-quinoline-1-oxide, diepoxybutane	Air	Multi
ak Ridge aboratory	--	4C1, 2B1, 5A1, 1A1	Cellular toxicology	Carcinogenesis	Injection, topical	Hamster	Diethylnitrosamine, NO_2, formaldehyde, acrolein	Air	GA
ak Ridge aboratory	--	4C1, 1A1, 2B1	Cellular toxicology	Cytotoxicity, carcinogenesis	Tissue culture media application	Various systems, incl. tracheal explants	Dimethylbenzanthracene	Air	GA
ence aboratory	--	4C1, 1A1, 3A1, 5A1	Animal toxicology	Carcinogenesis	Aerosol	Mouse lung	SO_2, NO_2, urethane	Air	GA
rence aboratory	--	4B2, 3A1, 3B3	Cellular toxicology	Toxicity	Aerosol	Lung	Particulates	Air	GA
rgonne aboratory	--	4C1, 1A1, 3B3, 5A1	Animal toxicology	Carcinogenesis	Per os	Rat liver	DDT, benz(a) anthracene, 2-acetylamino-fluorene	Multi	GA
EHS	8/75 - --	4B2, 4B3, 4C3	Animal toxicology	Teratogenesis	Inhalation	Mammals	Multiple pollutants	Multi	GA
IS	8/75 - --	4B2, 4B3, 5A1	Animal toxicology	Toxicity	Immersion	Mammals (CNS)	Electrical field	Multi	GA

TABLE A-1 (CONTINUED)

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JECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	E
piratory and Cardiovascular Functions in Pollutant osed Animals	NIEHS	Dixon (NIEHS)	VanStee, NIEHS	8/75 - --	4B2, 5A1	Animal toxicology	Toxi
ects of Gestational Exposure	NIEHS	Dixon (NIEHS)	Staples, NIEHS	8/75 - --	4C3, 1A3, 4D1	Animal toxicology	Tera
ine Toxicity: A Potential Environmental ard	NIEHS	Dixon (NIEHS)	Goldstein, New York University Medical Center	9/75 - 8/77	4B2, 4B3, 4C1, 3B1, 5A1, 5A2, 5B1	Animal toxicology	Toxi
d Toxicity and Energy Metabolism in ature Brain	NIEHS	Dixon (NIEHS)	Holtzman, Stanford University	9/75 - 8/78	4C3, 3B1, 5A1, 5A2	Cellular toxicology	Bioc cha
ding of Methyl Mercury, and Environmental ard, with DNA	NIEHS	Dixon (NIEHS)	Maki, University of California, Davis	9/75 - 8/77	4B3, 5A2	Cellular toxicology	Bioc cha
fects of Energy-Related Pollutants on avior	NIEHS	Dixon (NIEHS)	Mitchell, NIEHS	8/76 - --	4D1	Human health	Toxi
mical and Environmental Mutagen Studies ilizing the Tradescantia Test System	NIEHS	Malling (NIEHS)	Sparrow, Brookhaven National Laboratory	8/75 - --	4C3, 1A2, 3A1, 4C2, 5A2	Bioscreening, cellular toxicology	Muta
pilation and Tabular Abstracting of Literature Mutagenic Effects of Energy Related Pollutants	NIEHS	Malling (NIEHS)	Wassom, Oak Ridge National Laboratory	8/75 - --	4C2, 3B1, 3B2, 3B3, 5A2	Human health	Muta
ctrophoresis of Mouse Tissue: Testing of fspring after Parental Treatment with Energy ated Pollutants	NIEHS	Malling (NIEHS)	Johnson, Research Triangle Institute	8/75 - --	4C2	Animal toxicology	Muta
nitoring Mutagens (Clastogens) with Mammalian romosomes	NIEHS	Malling (NIEHS)	Hsu, University of Texas Cancer Center	7/76 - 6/81	4C2, 1A2	Cellular toxicology	Muta
velopment of Statistical Methodology for Low se Extrapolation	NIEHS	Hoel (NIEHS)	Guess, NIEHS	7/75 - --	4C1, 4D1	Risk/extrapolation	Can
ecies-to-Species Carcinogenesis Extrapolation	NIEHS	Hoel (NIEHS)	Williams, American Health Foundation	8/75 - --	4D1, 4C1	Risk/extrapolation	Can
atistical Studies of Problems of Health and ology	NIEHS	Hoel (NIEHS)	Neyman, NIEHS	9/75 - 8/78	4B1, 4C1	Risk/extrapolation	Toxi
trapolation of Polychlorinated Biphenyl position	NIEHS	Hoel (NIEHS)	Eling, NIEHS	8/75 - --	4D1	Risk/extrapolation	Toxi
meration of Energy Occupational Health Problems	NIOSH	Wagner (NIOSH)	Wagner, NIOSH-Morgantown	5/75 - 5/80	4A1	Risk/extrapolation	Toxi
rtality and Morbidity Among Oil Shale Workers	NIOSH	Wagner (NIOSH)	Gilliam, NIOSH-Morgantown	5/76 - 6/77	4A1	Risk/extrapolation	Toxi
neral Wool and Clay Fibers - Occupational Health idemiological Study	NIOSH	Wagner (NIOSH)	Dement, NIOSH-Cincinnati	1/74 - 9/78	4A1, 1A1, 1A4, 4A2, 4C1	Human health	Toxi
al Liquifaction and Gasification Studies	NIOSH	Wagner (NIOSH)	Hearl, NIOSH-Morgantown	--	4A1, 1A1, 1A4, 4A2	Human health	Toxi
rtality Study of TVA High Risk Workers	NIOSH	Wagner (NIOSH)	Ortmeyer, NIOSH-Morgantown	--	4A1, 3B3, 4B2, 4B1, 4C1	Human health	Toxi
lfuric Acid and Sulfates - Occupational Health idemiological Study	NIOSH	Wagner (NIOSH)	Cassady, NIOSH-Cincinnati	5/75 - 6/78	4A1, 3B3, 1A4, 2B1	Human health	Toxi
emical and Molecular Interactions of Pollutants th Key Biological Molecules*	ERDA	Jensen (ERDA)	Danyluk, Argonne National Laboratory	1/76 - 1/77	5A1, 3A1, 5A2	Cellular toxicology	Bio chi
lecular Damage of DNA and Proteins Caused by zardous Metals, Metal Ions and Organic Compounds Associated with Coal and Oil Shale chnologies*	ERDA	Jensen (ERDA)	Ward, UCLA Laboratory of Nuclear Medicine and Radiation Biology	1/77 - 7/77	5A1, 5A2	Cellular toxicology	Bio chi

NVESTI-IATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS, CHARACTERISTICS	MEDIUM	APPLICABL TECHNOLOG
EHS	8/75 - --	4B2, 5A1	Animal toxicology	Toxicity	Aerosol or perfusion	Cardiac (mammal)	Anesthetics, fluro-carbons, Br com-pounds	Multi	GA
EHS	8/75 - --	4C3, 1A3, 4D1	Animal toxicology	Teratogenesis	Aerosol	Mice, rabbits, hamsters	SO_2, pesticides, asbestos, noise	Multi	GA
New sity ter	9/75 - 8/77	4B2, 4B3, 4C1, 3B1, 5A1, 5A2, 5B1	Animal toxicology	Toxicity	Aerosol	Human red blood cells, cell cultures, E. coli	Arsine	Multi	GA
tan-sity	9/75 - 8/78	4C3, 3B1, 5A1, 5A2	Cellular toxi-cology	Biochemical changes	Per os	Rat brain	Pb	Multi	GA
rsity ia,	9/75 - 8/77	4B3, 5A2	Cellular toxi-cology	Biochemical changes	In vitro	Mammalian cells, Allium cepa cells	Methyl mercury	Multi	GA
IEHS	8/76 - --	4D1	Human health	Toxicity	Inhalation	Rat behavior (CNS)	Heavy metals, hydrocarbon pollutants	Multi	GA
ook-nal	8/75 - --	4C3, 1A2, 3A1, 4C2, 5A2	Bioscreening, cellular toxicology	Mutagenesis	Direct application	Tradescentia	Dibromoethane, CO, Vapona, sodium azide, other	Multi	GA
Ridge oratory	8/75 - --	4C2, 3B1, 3B2, 3B3, 5A2	Human health	Mutagenesis	N/A	N/A	Multiple pollutants	Multi	GA
search stitute	8/75 - --	4C2	Animal toxicology	Mutagenesis	Direct applica-tion	Mice	Irradiation	Multi	GA
sity of Center	7/76 - 6/81	4C2, 1A2	Cellular toxi-cology	Mutagenesis	Cell culture media	Mammalian cells	Clastogens	Multi	GA
	/75 - --	4C1, 4D1	Risk/extra-polation	Carcinogenesis	N/A	N/A	Multiple pollutants	Multi	GA
erican dation	8/75 - --	4D1, 4C1	Risk/extra-polation	Carcinogenesis	N/A	N/A	Multiple pollutants	Multi	GA
IS	9/75 - 8/78	4B1, 4C1	Risk/extra-polation	Toxicity	N/A	N/A	Multiple pollutants	Multi	GA
	8/75 - --	4D1	Risk/extra-polation	Toxicity	N/A	Organ deposition	PCBs	Multi	GA
H-	5/75 - 5/80	4A1	Risk/extra-polation	Toxicity	N/A	N/A	Multiple pollutants	Multi	GA
SH-	5/76 - 6/77	4A1	Risk/extra-polation	Toxicity	N/A	N/A	Multiple pollutants	Multi	GA
H-	1/74 - 9/78	4A1, 1A1, 1A4, 4A2, 4C1	Human health	Toxicity	Aerosol	Respiratory system	Mineral and clay fibers, multiple pollutants	Multi	GA
-	--	4A1, 1A1, 1A4, 4A2	Human health	Toxicity	Ambient air	Man-pulmonary	Multiple pollutants	Multi	Coal (g,l)
OSH-	--	4A1, 3B3, 4B2, 4B1, 4C1	Human health	Toxicity	Ambient air	Man-pulmonary	Multiple pollutants	Multi	Coal
SH-	5/75 - 6/78	4A1, 3B3, 1A4, 2B1	Human health	Toxicity	Industrial exposure	Man	Pollutants in paper and smelting industries	Multi	GA
onne oratory	1/76 - 1/77	5A1, 3A1, 5A2	Cellular toxi-cology	Biochemical changes	Tissue culture media applica-tion	Cell membranes, nucleic acids	Mercury, NO_x, SO_x, Cd, As, Be, aromatic carcinogens	Multi	GA
f cine n	1/77 - 7/77	5A1, 5A2	Cellular toxi-cology	Biochemical changes	In vitro	--	Hg, Mn	Multi	GA

TABLE A-1 (CONTINUED)

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PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HE END
The Study of Autoxidation of Lipids of Biomembranes and of Lung Surfactants Initiated by Oxidative Pollutants and Its Inhibition by Antioxidants*	ERDA	Jensen (ERDA)	Mead, UCLA Laboratory of Nuclear Medicine and Radiation Biology	1/76 - 1/77	5A1, 5A2	Cellular toxicology	Biochem changes
Effect of Hydrocarbons, SO_2, and Related Fossil Fuel Pollutants on the Biochemical Properties of Lung Membranes During Development*	ERDA	Jensen (ERDA)	Snyder, Oak Ridge Association Universities	--	5A1, 5A2	Cellular toxicology	Biochem changes
Effects of Hazardous Agents Associated with Coal and Oil Shale Technologies on Informational and Regulatory Macromolecules of Mammalian Cells*	ERDA	Jensen (ERDA)	Enger, Los Alamos Scientific Laboratory	--	5A2	Cellular toxicology	Toxicit biochem changes
Damage to DNA Synthesis by Trace Metals and Hydrocarbons*	ERDA	Jensen (ERDA)	Popenoe, Argonne National Laboratory	--	5A2, 2B2	Cellular toxicology	Toxicit biochem changes
Molecular Mechanisms of Chemical Carcinogenesis*	ERDA	Jensen (ERDA)	Calvin, Lawrence Berkeley Laboratory	--	5A2	Cellular toxicology	Carcino
Characterization and Control of Frameshift Mutations*	ERDA	Jensen (ERDA)	Tinoco, Lawrence Berkeley Laboratory	--	5A2, 4C1, 4C2	Cellular toxicology	Mutagen carcino
Characterization of Damage to DNA Caused by Chemical Agents: Emphasis on Synergistic Effects in Combination with Sunlight*	ERDA	Jensen (ERDA)	Rahn, Oak Ridge National Laboratory	1/76 - 1/77	5A2	Cellular toxicology	Biochem changes
Regulatory Processes in Damaged Cells*	ERDA	Jensen (ERDA)	Kenney, Oak Ridge National Laboratory	7/76 - 7/77	5A2	Cellular toxicology	Biochem changes
Damage and Repair to DNA in Specific Germ Cell Stages of Mammals Following in vivo Exposure to Products Associated with Coal Conversion and Utilization*	ERDA	Jensen (ERDA)	Sega, Oak Ridge National Laboratory	7/76 - 7/77	5A2, 5B1	Cellular toxicology	Mutagen biochem changes
Interactions Between Damage (and Repair to Damage) Resulting from Hazardous Agents Associated with Coal and Oil Shale Technologies and Ultraviolet Damage*	ERDA	Jensen (ERDA)	Setlow, Brookhaven National Laboratory	--	5B1, 5B2, 5A2	Cellular toxicology	Carcino biochem changes
Damage-Repair Studies Related to Cell Function and Molecular Processes*	ERDA	Jensen (ERDA)	Elkind, Argonne National Laboratory	1/76 - 7/77	5A2, 5B1	Cellular toxicology	Biochem changes
Repair of DNA Treated with Irradiation and Chemical Carcinogens*	ERDA	Jensen (ERDA)	Goldthwait, Case Western Reserve Institute	--	5A2, 5B1	Cellular toxicology	Carcino
Biological Damage Processes of Hydrocarbons; Molecular Activation and Binding Evaluated by EPR and the Development of a Chemical Screening Test for Potential Carcinogenicity/Mutagenicity*	ERDA	Jensen (ERDA)	Borg, Brookhaven National Laboratory	1/76 - 1/77	5A2, 1A1, 1A2	Cellular toxicology	Carcino mutagen
Reparative and Adaptive Mechanisms in Respiratory Systems of Rodents and Monkeys Exposed to Sulfur Compounds and Particulates*	ERDA	Minthorn (ERDA)	Goldman, University of California, Davis	--	5B1, 5B2, 5A1	Cellular toxicology	Toxici
Lung Cell Injury and Repair After Inhalation Exposure to Particulate Acid Sulphates*	ERDA	Minthorn (ERDA)	Slauson, Lovelace Foundation	1/76 - 1/78	5A1, 5B1, 4B2	Cellular toxicology	Toxici
Alveolar Clearance of Inhaled Metal Oxides*	ERDA	Minthorn (ERDA)	Sanders, Battelle, Pacific Northwest Laboratories	1/76 - 7/80	5B2, 1A4, 3A1, 4B2	Cellular toxicology	Toxici
Effects of Chemical Toxicants Associated with the Production and Consumption of Fuel on the Physiology and Pathophysiology of Phagocytic Cells*	ERDA	Minthorn (ERDA)	Skosey, Franklin McLean Memorial Research Institute; University of Chicago	--	5A1	Cellular toxicology	Toxici
Evaluation of the Mechanisms of Energy-Related Toxic Agents on the Mammalian Hematopoietic System Using Flow Microfluorometric Analysis*	ERDA	Minthorn (ERDA)	Steinkamp, Los Alamos Scientific Laboratory	--	5A1, 2B1, 5A2, 1A4	Bioscreening, cellular toxicology	Toxici

STI-ION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATION	TARGET/TISSUE OF CONCERN	AGENTS CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
ne	1/76 - 1/77	5A1, 5A2	Cellular toxicology	Biochemical changes	In vitro	Lung, liver, other cells	NO_2, O_3	Multi	GA
dge	--	5A1, 5A2	Cellular toxicology	Biochemical changes	In vitro	Lung	NO_2	Multi	GA
mos	--	5A2	Cellular toxicology	Toxicity, biochemical changes	Tissue culture media application	Mammalian cells	Cd	Multi	GA
ne	--	5A2, 2B2	Cellular toxicology	Toxicity, biochemical changes	In vitro	Mammalian cells, DNA, DNA polymerases	Hg, Cu, Pb, PNH	Multi	GA
ce a-	--	5A2	Cellular toxicology	Carcinogenesis	In vitro	--	Benzo(α) pyrene	Multi	GA
ce a-	--	5A2, 4C1, 4C2	Cellular toxicology	Mutagenesis, carcinogenesis	Bacterial culture media application	Salmonella	Non-mutagenic and mutagenic F compounds	Multi	GA
e a-	1/76 - 1/77	5A2	Cellular toxicology	Biochemical changes	In vitro	DNA	PCH, organic peroxides, irradiation	Multi	GA
dge a-	7/76 - 7/77	5A2	Cellular toxicology	Biochemical changes	In vitro	Mouse hepatoma cells, embryo cells	Benzo(α) pyrene, DMBA	Multi	GA
e a-	7/76 - 7/77	5A2, 5B1	Cellular toxicology	Mutagenesis, biochemical changes	In vitro	Mammalian germ cells	Benzo(α) pyrene, DMBA	Multi	Coal
	--	5B1, 5B2, 5A2	Cellular toxicology	Carcinogenesis biochemical changes	In vitro	Bacterial and mammalian cells	Dichloromethane, a-acetoxy-AAF, UV radiation	Multi	Coal, oil shale
e	1/76 - 7/77	5A2, 5B1	Cellular toxicology	Biochemical changes	Tissue culture media application	Mammalian cells	UV light	Air	Solar
se e	--	5A2, 5B1	Cellular toxicology	Carcinogenesis	Tissue culture media application	Cell cultures	EndonucleaseII, gamma-irradiation, methylmethane sulfonate	Multi	GA
en a-	1/76 - 1/77	5A2, 1A1, 1A2	Cellular toxicology	Carcinogenesis, mutagenesis	Cell culture media application	Nucleic acids	--	Multi	GA
r- rnia,	--	5B1, 5B2, 5A1	Cellular toxicology	Toxicity	Aerosol	Rodent, nonhuman primate respiratory tracts	H_2SO_4, SiO_2, fly ash	Air	GA
ace	1/76 - 1/78	5A1, 5B1, 4B2	Cellular toxicology	Toxicity	Aerosol	Lung cells	Multiple pollutants	Air	Coal
lle, est	1/76 - 7/80	5B2, 1A4, 3A1, 4B2	Cellular toxicology	Toxicity	Aerosol	Hamsters, rats, pulmonary cells	Cd^{+2}, Zn^{+2}, Pb, Hg	Air	GA
in l tute;	--	5A1	Cellular toxicology	Toxicity	--	Phagocytic cells	Multiple pollutants	Air	GA
fic	--	5A1, 2B1, 5A2, 1A4	Bioscreening, cellular toxicology	Toxicity	Aerosol	Lung cells, blood cells	Particulates	Air	Fossil Fuel

TABLE A-1 (CONTINUED)

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PROJECT NUMBER AND TITLE	PERFORMING AGENCY	PROJECT OFFICER	PRINCIPAL INVESTIGATOR/AFFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEA END
Functional and Quantitative Changes in Immunocompetent Cells, Induced by a Carcinogenic Product of Coal and Oil Utilization*	ERDA	Minthorn (ERDA)	Jaroslow, Argonne National Laboratory	--	5A2, 4B2, 4C1, 5B2	Cellular toxicology	Carci
Environmental Carcinogenic Studies in a Primate Known to have a High Incidence of Spontaneous Cancer*	ERDA	Minthorn (ERDA)	Gengozian, Oak Ridge Association Universities	1/76 - 1/77	5B1, 5B2	Cellular toxicology	Carci
To Determine the Processes by which Laboratory Mammals Recover from Damage by Exposure to Pollutants Associated with Coal Gasification and Shale Distillation with Emphasis on the Sequence of Events Occurring in the Immune System*	ERDA	Minthorn (ERDA)	Smith, Los Alamos Scientific Laboratory	--	5B2, 4B2, 4D1	Cellular toxicology	Biochc chang
Evaluation of the Dose-Effect Relationships for the Immune Response to Biologically Active Agents Associated with Coal Gasification Technologies*	ERDA	Minthorn (ERDA)	Cram, Los Alamos Scientific Laboratory	1/76 - 1/77	5A1, 2B1, 4B2	Cellular toxicology	Toxic
Therapy of Non-Radioactive Toxic Metal Compounds*	ERDA	Minthorn (ERDA)	Lindenbaum, Argonne National Laboratory	1/76 - 7/78	5A2, 5C2, 3A1, 4D1	Cellular toxicology	Toxic
Effects of Pollutants upon Alveolar Macrophages	NIEHS	Hart (NIEHS)	Rowlands, Southwest Foundation for Research and Education	6/75 - 5/77	5A2, 3B3, 4B2, 5A1	Cellular toxicology	Toxic
Can Vitamin E or Lipid Alter NO_2 or O_3 Toxicity in Lung?	NIEHS	Hart (NIEHS)	Menzel, Duke University Medical Center	9/75 - 8/78	5B1, 5C1, 4B3	Cellular toxicology	Toxic
Vitamin A Effect on Lung Cell Cycle Kinetics after NO_2	NIEHS	Hart (NIEHS)	Kim, Michigan State University	9/75 - 8/77	5B1, 5C1	Cellular toxicology	Toxic
The Interaction of Cadmium with the Pulmonary Alveolar Macrophage	NIEHS	Hart (NIEHS)	Hart, University of Vermont	9/75 - 8/77	5A2, 4B2, 3B1 3A1	Cellular toxicology	Toxic
Pulmonary Effects of Environmental Oxidant Pollutants	NIEHS	Hart (NIEHS)	Dungworth, University of California, Davis	9/75 - 8/78	5A2, 2B1, 2B2, 2B3, 5B1	Cellular toxicology	Toxic
Environmental Cellular Toxicology Program	NIEHS	Hart (NIEHS)	Wenzel, University of Kansas	4/77 - 3/80	5A1	Cellular toxicology	Toxic
Development of Criteria for Recirculation of Exhaust Air	NIOSH	Wagner (NIOSH)	Hughes, NIOSH - Cincinnati	7/73 - 3/78	5C2, 1A4	Human health	Toxic
Cold Stress Associated with the Alaskan Pipeline	NIOSH	Wagner (NIOSH)	Wagner, NIOSH - Salt Lake City; NIOSH - Cincinnati	--	5C1, 5D2	Human health	Toxic
Development of Countermeasures to Protect Divers	NIOSH	Wagner (NIOSH)	Fairchild, NIOSH - Cincinnati; NIOSH - Morgantown	5/75 - 5/80	5D1, 5D2	Human health	Toxic
Recommended Standards for Coal Gasification Plants	NIOSH	Wagner (NIOSH)	Cohen, NIOSH - Rockville	--	5C2, 5D1	Human health	Toxic
Develop Analytical Methods to Determine OCC Exposure to H_2SO_4 Sulfate, Sulfite, HNO_3, and NO_2	NIOSH	Wagner (NIOSH)	Haartz, NIOSH - Cincinnati	--	5D1, 1A4	Human health	Toxic
Development and Fabrication of a Prototype Portable Microwave Spectrometer Analyzer	NIOSH	Wagner (NIOSH)	Baron, NIOSH - Cincinnati	--	5D1	Human health	Toxic

AL INVESTI-FFILIATION	PLANNED PERIOD OF PERFORMANCE	K/M SUB-OBJECTIVE	DISCIPLINE APPROACHES	HEALTH END POINTS	ROUTES OF ADMINISTRATIVE	TARGET/TISSUE OF CONCERN	AGENTS CHARACTERISTICS	MEDIUM	APPLICABLE TECHNOLOGY
w, Argonne l Labora-	--	5A2, 4B2, 4C1, 5B2	Cellular · toxicology	Carcinogenesis	Injection	Mice	3-Methyl-cholanthrene	Multi	Coal, oil shale
an, Oak ssociation ities	1/76 - 1/77	5B1, 5B2	Cellular toxi-cology	Carcinogenesis	Per os	Marmosets	PCB	Water	GA
Los Alamos fic Labora-	--	5B2, 4B2, 4D1	Cellular toxi-cology	Biochemical changes	Aerosol	Rats, hamsters	Multiple com-pound aerosols	Air	Coal, oil shale
os Alamos fic ory	1/76 - 1/77	5A1, 2B1, 4B2	Cellular toxi-cology	Toxicity	Tissue culture media applica-tion	Human and hamster lymphocytes	Multiple pollutants	Multi	Coal, oil shale
um, Argonne l Laboratory	1/76 - 7/78	5A2, 5C2, 3A1, 4D1	Cellular toxi-cology	Toxicity	Injection, in vitro	Mice, dogs	Pb	Multi	--
, Southwest lon for Re-and Education	6/75 - 5/77	5A2, 3B3, 4B2, 5A1	Cellular toxi-cology	Toxicity	Aerosol	Alveolar macro-phage	SO_2	Multi	GA
Duke Univer-lical Center	9/75 - 8/78	5B1, 5C1, 4B3	Cellular toxi-cology	Toxicity	Aerosol	Mouse lung	O_3, Vit. E	Multi	GA
chigan State ity	9/75 - 8/77	5B1, 5C1	Cellular toxi-cology	Toxicity	Per os	Hamster lung	NO_2, Vit. A	Multi	GA
niversity ent	9/75 - 8/77	5A2, 4B2, 3B1 3A1	Cellular toxi-cology	Toxicity	Tissue culture media applica-tion	Guinea pig lung	Cd	Multi	GA
h, Univer-California,	9/75 - 8/78	5A2, 2B1, 2B2, 2B3, 5B1	Cellular toxi-cology	Toxicity	Aerosol	Rats, monkeys	O_3	Multi	GA
University s	4/77 - 3/80	5A1	Cellular toxi-cology	Toxicity	Tissue culture media applica-	Cells of blood, nerve, lung, heart, and endothelium	Multiple pollutants	Multi	GA
NIOSH - ti	7/73 - 3/78	5C2, 1A4	Human health	Toxicity	N/A	N/A	Multiple pollutants	Multi	Conserva-tion
NIOSH - e City; Cincinnati	--	5C1, 5D2	Human health	Toxicity	N/A	Workers on Alaskan pipe-line	Cold stress	Air	Oil
d, NIOSH - ti; NIOSH - wn	5/75 - 5/80	5D1, 5D2	Human health	Toxicity	N/A	N/A	None	Water	GA
IOSH - e	--	5C2, 5D1	Human health	Toxicity	N/A	N/A	Multiple pollutants	Multi	GA
NIOSH - ti	--	5D1, 1A4	Human health	Toxicity	Aerosol	Monitor	HNO_3, NO_2, H_2SO_4, SO_3	Multi	GA
IOSH - ti	--	5D1	Human health	Toxicity	N/A	Monitor	N/A	Multi	GA

TABLE A-1 (CONCLUDED)

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TABLE A-2 INTERAGENCY ENERGY/ENVIRONMENT HEALTH EFFECTS RELATED R&D PROGRAM; KING-MUIR OBJECTIVE AREAS*

OBJECTIVE 1: To identify hazardous agents associated with energy technologies.

- A. Use existing and new biological screening and testing systems to determine the presence of hazardous agents.
  1. Use systems to determine the presence of carcinogenic agents.
  2. Use systems to determine the presence of mutagenic agents.
  3. Use systems to determine the presence of teratogenic agents.
  4. Use systems to determine the presence of physiologically and metabolically toxic agents.

OBJECTIVE 2: To develop more sensitive and rapid biological methods to evaluate dose and dosage to man.

- A. Develop cytological, biochemical and physiological indicators to estimate dose to man.
  1. Develop better analytical techniques for quantitating tissue residues of toxic agents.
  2. Develop cytological indicators to estimate dose to man.
  3. Develop biochemical and physiological indicators to estimate dose to man.
- B. Develop cytological, biochemical and physiological indicators to estimate damage to man.
  1. Develop cytological indicators to estimate damage to man.
  2. Develop biochemical indicators to estimate damage to man.
  3. Develop physiological indicators to estimate damage to man.

OBJECTIVE 3: To determine the metabolism and fate of hazardous agents associated with energy technologies.

- A. Determine the mechanisms and kinetics of incorporation, metabolism, deposition and turnover of hazardous agents.
  1. Determine the mechanisms of incorporation, metabolism, deposition and turnover of hazardous agents.
- B. Determine the relationship of metabolism and fate of hazardous agents to the expression of health effects.
  1. Determine the relationship of metabolism and fate and the toxicology of trace elements and inorganic compounds.
  2. Determine the relationship of metabolism and fate and the toxicology of nuclear fuel components and by-products.
  3. Determine the relationship of metabolism and fate and the toxicology of particulates and organic compounds.

OBJECTIVE 4: To evaluate the short-term and long-term hazards of exposure of normal, susceptible and stressed population groups to different levels and combinations of biologically active agents associated with energy technologies.

- A. Conduct epidemiological and clinical studies in selected human population groups to evaluate the hazards of exposure to biologically active agents.
  1. Conduct epidemiological studies in selected human population groups.
  2. Conduct clinical studies in selected human population groups.
- B. Determine the dose-effect relationships for diverse behavioral, physiological and metabolic effects resulting from exposure to hazardous agents.
  1. Determine the dose-effect relationships for life-shortening effects.
  2. Determine the dose-effect relationships for physiological effects.
  3. Determine the dose-effect relationships for metabolic effects.
- C. Determine the dose-effect relationships for mutagenicity, carcinogenicity and teratogenicity for specific hazardous agents, using selected cellular and animal models, to assist in the determination of acceptable human exposure levels.
  1. Determine the dose-effect relationships for carcinogenic agents.
  2. Determine the dose-effect relationships for mutagenic agents.
  3. Determine the dose-effect relationships for teratogenic agents.
- D. Improve models and concepts for extrapolation of cellular and animal data to man.
  1. Develop and test models and extrapolation of cellular and animal data to man.

OBJECTIVE 5: To determine the processes of damage, repair, recovery, protection and amelioration in biological systems exposed to hazardous agents associated with energy technologies.

- A. Identify the biochemical lesions induced by interactions of biological systems with hazardous agents in order to identify susceptible population sub-groups, provide early indicators of injury, and guide the development of protective and remedial therapies.
  1. Identify damage to cells and cell components.
  2. Identify molecular changes which cause damage.
- B. Identify the mechanisms by which living systems repair and recover from lesions induced by exposure to hazardous agents, and assess the role of these mechanisms in human resistance of these agents.
  1. Identify the mechanisms by which living systems repair damage.
  2. Identify the mechanisms by which living systems recover from damage.
- C. Develop and test methods to enhance natural human recovery and repair mechanisms, and develop protective and remedial therapies.
  1. Develop and test methods to enhance cell replacement and recovery.
  2. Develop and test methods for removing hazardous agents from exposed individuals.
- D. Develop and test devices and procedures to protect against effects of hazardous agents, particularly in the occupational setting.
  1. Develop engineering control methods and test control devices for worker protection.
  2. Develop and test countermeasures to protect workers.

*From Final Report of the Interagency Working Group on Health and Environmental Effects of Energy Use (King-Muir Report), prepared for OMB and CEQ, November, 1974.

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